Clinical trial results:
A Phase 2b Dose Ranging Study to Evaluate the Efficacy and Safety of Efavaleukin Alfa in Subjects With Active Systemic Lupus Erythematosus With Inadequate Response to Standard of Care Therapy (VIOLET)

Summary

EudraCT number	2020-003509-72
Trial protocol	FR GR PL AT BG ES IT
Global end of trial date	24 May 2023

Results information

Result version number	v1 (current)
This version publication date	07 June 2024
First version publication date	07 June 2024

Trial information

Trial identification

Sponsor protocol code	20200234

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04680637
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States,
Public contact	Study Director, Amgen Inc., +1 8665726436, medinfo@amgen.com
Scientific contact	Study Director, Amgen Inc., +1 8665726436, medinfo@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	24 May 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 May 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to evaluate the efficacy of efavaleukin alfa at Week 52, as measured by the Systemic Lupus Erythematosus Responder Index 4 (SRI-4) response.

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP) and with consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines.

Background therapy:

Participants were permitted to receive immunosuppressants/immunomodulators, oral corticosteroids, topical corticosteroids and topical calcineurin inhibitors, non-steroidal anti-inflammatory drugs (NSAIDS) and other analgesic therapies and anti-proteinuria agents, as outlined in the protocol and based upon clinical judgment of the investigator.

Evidence for comparator: -

Actual start date of recruitment	06 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	Bulgaria: 17
Country: Number of subjects enrolled	Chile: 14
Country: Number of subjects enrolled	Colombia: 12
Country: Number of subjects enrolled	Greece: 6
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Japan: 10
Country: Number of subjects enrolled	Mexico: 21
Country: Number of subjects enrolled	Poland: 14
Country: Number of subjects enrolled	Russian Federation: 2
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	Switzerland: 5
Country: Number of subjects enrolled	Taiwan: 9
Country: Number of subjects enrolled	United States: 53
Worldwide total number of subjects	168
EEA total number of subjects	42

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)	160
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 73 centers in 13 countries (Bulgaria, Chile, Colombia, Greece, Italy, Japan, Mexico, Poland, Russian Federation, Spain, Switzerland, Taiwan, and the United States) between 06 May 2021 and 24 May 2023.

Pre-assignment

Screening details:

A total of 464 participants were screened, of which 168 participants were enrolled and received efavaleukin alfa.

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 received placebo matching efavaleukin alfa every two weeks (Q2W) through a subcutaneous (SC) injection for up to 52 weeks.

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

Dosage and administration details:

Placebo matching efavaleukin alfa Q2W for up to 52 weeks.

Arm title	Efavaleukin Alfa Low Dose

Arm description:

Participants received low dose efavaleukin alfa Q2W through a SC injection for up to 52 weeks.

Arm type	Experimental
Investigational medicinal product name	Efavaleukin Alfa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Low dose Q2W for up to 52 weeks.

Arm title	Efavaleukin Alfa Medium Dose

Arm description:

Participants received medium dose efavaleukin alfa Q2W through a SC injection for up to 52 weeks.

Arm type	Experimental

Investigational medicinal product name	Efavaleukin Alfa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Medium dose Q2W for up to 52 weeks.

Arm title	Efavaleukin Alfa High Dose

Arm description:

Participants received high dose efavaleukin alfa Q2W through a SC injection for up to 52 weeks.

Arm type	Experimental
Investigational medicinal product name	Efavaleukin Alfa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

High dose Q2W for up to 52 weeks.

Number of subjects in period 1	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose
Started	41	35	34
Received Study Treatment	41	35	34
Completed	12	9	10
Not completed	29	26	24
Adverse event, serious fatal	1	-	-
Consent withdrawn by subject	7	10	17
Decision by Sponsor	21	15	7
Lost to follow-up	-	1	-

Number of subjects in period 1	Efavaleukin Alfa High Dose
Started	58
Received Study Treatment	58
Completed	10
Not completed	48
Adverse event, serious fatal	-
Consent withdrawn by subject	15
Decision by Sponsor	32
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo matching efavaleukin alfa every two weeks (Q2W) through a subcutaneous (SC) injection for up to 52 weeks.	
Reporting group title	Efavaleukin Alfa Low Dose
Reporting group description:	
Participants received low dose efavaleukin alfa Q2W through a SC injection for up to 52 weeks.	
Reporting group title	Efavaleukin Alfa Medium Dose
Reporting group description:	
Participants received medium dose efavaleukin alfa Q2W through a SC injection for up to 52 weeks.	
Reporting group title	Efavaleukin Alfa High Dose
Reporting group description:	
Participants received high dose efavaleukin alfa Q2W through a SC injection for up to 52 weeks.	

Reporting group values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose
Number of subjects	41	35	34
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational 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
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	39	31	33
From 65-84 years	2	4	1
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	48.1	46.1	40.3
standard deviation	± 10.3	± 12.8	± 12.2
Sex: Female, Male Units:			
Female	38	31	33
Male	3	4	1
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	14	11	12
Not Hispanic or Latino	27	24	22
Unknown or Not Reported	0	0	0
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	4	2	3
Asian	6	2	5

Black (or African American)	5	8	1
Multiple	0	0	1
White	25	20	20
Other	1	3	4

Reporting group values	Efavaleukin Alfa High Dose	Total	
Number of subjects	58	168	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	57	160	
From 65-84 years	1	8	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	42.3		
standard deviation	± 11.2	-	
Sex: Female, Male Units:			
Female	56	158	
Male	2	10	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	22	59	
Not Hispanic or Latino	36	109	
Unknown or Not Reported	0	0	
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	5	14	
Asian	6	19	
Black (or African American)	9	23	
Multiple	0	1	
White	29	94	
Other	9	17	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received placebo matching efavaleukin alfa every two weeks (Q2W) through a subcutaneous (SC) injection for up to 52 weeks.	
Reporting group title	Efavaleukin Alfa Low Dose
Reporting group description:	
Participants received low dose efavaleukin alfa Q2W through a SC injection for up to 52 weeks.	
Reporting group title	Efavaleukin Alfa Medium Dose
Reporting group description:	
Participants received medium dose efavaleukin alfa Q2W through a SC injection for up to 52 weeks.	
Reporting group title	Efavaleukin Alfa High Dose
Reporting group description:	
Participants received high dose efavaleukin alfa Q2W through a SC injection for up to 52 weeks.	

Primary: Number of Participants Who Achieved an SRI-4 Response at Week 52

End point title	Number of Participants Who Achieved an SRI-4 Response at Week 52[1]

End point description:

A participant achieved an SRI-4 response if all the following criteria were met:
- ≥ 4-point reduction from baseline in Hybrid Systemic Lupus Erythematosus Disease Activity Index (hSLEDAI) score (scale 0-105, with higher scores indicating more disease activity).
- No new British-Isles Lupus Assessment Group (BILAG) A score and no > 1 new BILAG B organ domain scores compared with baseline. The BILAG index evaluates disease activity in 9 separate organ systems. Each of the organ systems are allocated an alphabetical score of A (most active), B (moderate activity), C (minor activity), D (stable) or E (never present).
- < 0.3-points deterioration from baseline in Physician Global Assessment (PGA) visual analogue (VAS) score (scale 0 to 3, with higher scores indicating more severe disease).

Participants were considered non-responders for using more than protocol-permitted therapies.

Full Analysis Set: Included all participants randomized in the study.

End point type	Primary

End point timeframe:

Week 52

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: No statistical analysis was planned for this endpoint.

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15[2]	16[3]	17[4]	14[5]
Units: participants	8	4	6	5

Notes:

[2] - Participants who completed visit by date of termination decision communication were included.

[3] - Participants who completed visit by date of termination decision communication were included.

[4] - Participants who completed visit by date of termination decision communication were included.

[5] - Participants who completed visit by date of termination decision communication were included.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Achieved a Lupus Low Disease Activity State (LLDAS) Response at Week 52

End point title	Number of Participants Who Achieved a Lupus Low Disease Activity State (LLDAS) Response at Week 52

End point description:

A participant achieved an LLDAS response if all the following criteria were met:
- hSLEDAI ≤ 4 (scale 0-105, higher scores indicating more disease activity) with no activity in major organ systems (renal, central nervous system, cardiopulmonary, vasculitis and fever) & no hemolytic anemia or gastrointestinal activity in BILAG. The BILAG index evaluates disease activity in 9 separate organ systems. Each of the organ systems are allocated an alphabetical score of A (most active) to E (never present).
- No new lupus disease activity compared with previous assessment defined as no new descriptor scores in hSLEDAI.
- A score of < 1 in PGA VAS score (scale 0 to 3, with higher scores indicating more severe disease).
- Current prednisolone dose ≤ 7.5 mg daily.
- No increase or initiation of immunosuppressive drugs.

Participants were considered non-responders for using more than protocol-permitted therapies.

End point type	Secondary

End point timeframe:

Week 52

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15[6]	16[7]	17[8]	14[9]
Units: participants	2	3	3	1

Notes:

[6] - FAS: Participants who completed visit by date of termination decision communication were included.

[7] - FAS: Participants who completed visit by date of termination decision communication were included.

[8] - FAS: Participants who completed visit by date of termination decision communication were included.

[9] - FAS: Participants who completed visit by date of termination decision communication were included.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Achieved a BILAG-based Composite Lupus Assessment (BICLA) Response at Week 52

End point title	Number of Participants Who Achieved a BILAG-based Composite Lupus Assessment (BICLA) Response at Week 52

End point description:

A participant achieved a BICLA response if all the following criteria were met:
- At least 1 gradation of improvement in baseline BILAG domain scores in all body systems with moderate or severe disease activity at entry and no > 1 BILAG B domain scores compared with baseline. The BILAG index evaluates disease activity in 9 separate organ systems. Each of the organ systems are allocated an alphabetical score of A (most active), B (moderate activity), C (minor activity), D (stable) or E (never present).
- No worsening of the hSLEDAI score from baseline (scale 0-105, with higher scores indicating more disease activity).
- < 0.3-points deterioration from baseline in PGA VAS (scale 0 to 3, with higher scores indicating more severe disease).
- No initiation of non-protocol treatment.

Full Analysis Set: Included all participants randomized in the study. Participants were considered non-responders for using more than protocol-permitted therapies.

End point type	Secondary

End point timeframe:

Week 52

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15[10]	16[11]	17[12]	14[13]
Units: participants	6	2	4	4

Notes:

[10] - Participants who completed visit by date of termination decision communication were included.

[11] - Participants who completed visit by date of termination decision communication were included.

[12] - Participants who completed visit by date of termination decision communication were included.

[13] - Participants who completed visit by date of termination decision communication were included.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Achieved a BICLA Response at Week 24

End point title	Number of Participants Who Achieved a BICLA Response at Week 24

End point description:

A participant achieved a BICLA response if all the following criteria were met:
- At least 1 gradation of improvement in baseline BILAG domain scores in all body systems with moderate or severe disease activity at entry and no > 1 BILAG B domain scores compared with baseline. The BILAG index evaluates disease activity in 9 separate organ systems. Each of the organ systems are allocated an alphabetical score of A (most active), B (moderate activity), C (minor activity), D (stable) or E (never present).
- No worsening of the hSLEDAI score from baseline (scale 0-105, with higher scores indicating more disease activity).
- < 0.3-points deterioration from baseline in PGA VAS (scale 0 to 3, with higher scores indicating more severe disease).
- No initiation of non-protocol treatment.

Full Analysis Set: Included all participants randomized in the study.

End point type	Secondary

End point timeframe:

Week 24

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34[14]	29[15]	31[16]	44[17]
Units: participants	17	12	5	17

Notes:

[14] - Participants who completed visit by date of termination decision communication were included.

[15] - Participants who completed visit by date of termination decision communication were included.

[16] - Participants who completed visit by date of termination decision communication were included.

[17] - Participants who completed visit by date of termination decision communication were included.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with a Reduction of Oral Corticosteroids (OCS) to ≤ 7.5 mg/day by Week 44 and Sustained Through Week 52 in Participants with a Baseline OCS Dose ≥ 10 mg/day

End point title	Number of Participants with a Reduction of Oral Corticosteroids (OCS) to ≤ 7.5 mg/day by Week 44 and Sustained Through Week 52 in Participants with a Baseline OCS Dose ≥ 10 mg/day

End point description:

Participants taking OCS could begin tapering OCS after the Week 12 assessment up to the Week 44 assessment with initiation of tapering based upon clinical judgement of the treating physician. The tapering schedule was at the discretion of the investigator but should not have been tapered more than 20% of the prior dose per week. Tapering OCS before Week 12 was not encouraged but may have been allowed based upon investigator's judgement. Between Weeks 44 and 52, the OCS dosing must again have remained stable.

Full Analysis Set: Included all participants randomized in the study. Only participants with a baseline OCS dose ≥ 10 mg/day and had the opportunity to complete the visit by the date of the study termination decision being communicated to sites were included.

End point type	Secondary

End point timeframe:

Baseline to Week 52

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	9	8	7
Units: participants	0	1	2	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Achieved a SRI-4 Response at Week 24

End point title	Number of Participants Who Achieved a SRI-4 Response at Week 24

End point description:

A participant achieved an SRI-4 response if all the following criteria were met:
- ≥ 4-point reduction from baseline in hSLEDAI score (scale 0-105, with higher scores indicating more disease activity).
- No new BILAG A score and no > 1 new BILAG B organ domain scores compared with baseline. The BILAG index evaluates disease activity in 9 separate organ systems. Each of the organ systems are allocated an alphabetical score of A (most active), B (moderate activity), C (minor activity), D (stable) or E (never present).
- < 0.3-points deterioration from baseline in PGA VAS score (scale 0 to 3, with higher scores indicating more severe disease).

Participants were considered non-responders for using more than protocol-permitted therapies.

Full Analysis Set: Included all participants randomized in the study. Only participants who had the opportunity to complete the visit by the date of the study termination decision being communicated to sites were included.

End point type	Secondary

End point timeframe:

Week 24

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	29	31	44
Units: participants	20	13	13	21

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with an Improvement From Baseline in Tender and Swollen Joint Count ≥ 50% at Weeks 8, 12, 24, 36, and 52 in Participants with ≥ 6 Tender and Swollen Joints in Hands and Wrists

End point title	Number of Participants with an Improvement From Baseline in Tender and Swollen Joint Count ≥ 50% at Weeks 8, 12, 24, 36, and 52 in Participants with ≥ 6 Tender and Swollen Joints in Hands and Wrists

End point description:

The swollen and tender join count assessments were performed at the site by an experienced independent and blinded joint evaluator.

Each joint in hands and wrists were scored for the simultaneous presence (1) or absence (0) of swelling and tenderness. Scores ranged from 0-28. A higher score indicates more severe disease.

Full Analysis Set: Full Analysis Set: Included all participants randomized in the study. Only participants who had ≥ 6 tender and swollen joints involving hands and wrists at baseline and the opportunity to complete the visit by the date of the study termination decision being communicated to sites were included.

End point type	Secondary

End point timeframe:

Weeks 8, 12, 24, 36 and 52

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22[18]	16[19]	20[20]	27[21]
Units: participants				
Week 8	16	8	8	13
Week 12	16	7	7	13
Week 24	13	9	9	11
Week 36	11	8	8	3
Week 52	2	1	7	3

Notes:

[18] - Week 12 N = 22
Week 24 N = 19
Week 36 N = 26
Week 52 N = 8
[19] - Week 12 N = 14
Week 24 N = 13
Week 36 N = 13
Week 52 N = 7
[20] - Week 12 N = 19
Week 24 N = 18
Week 36 N = 17
Week 52 N = 12
[21] - Week 12 N = 25
Week 24 N = 20
Week 36 N = 8
Week 52 N = 4

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with a hSLEDAI Response at Week 24 and Week 52

End point title	Number of Participants with a hSLEDAI Response at Week 24 and Week 52

End point description:

The hSLEDAI is a global index that evaluates disease activity and includes both laboratory and clinical parameters. The score ranges from 0 to 105, with higher scores indicating more disease activity.

A participant achieved a hSLEDAI response if there was a ≥ 4-point reduction in hSLEDAI from baseline.

Full Analysis Set: Included all participants randomized in the study. Only participants who had the opportunity to complete the visit by the date of the study termination decision being communicated to sites were included.

End point type	Secondary

End point timeframe:

Week 24 and Week 52

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34[22]	29[23]	31[24]	44[25]
Units: participants				
Week 24	23	14	13	23
Week 52	8	4	7	6

Notes:

[22] - Week 52 N = 15

[23] - Week 52 N = 16

[24] - Week 52 N = 17

[25] - Week 52 N = 14

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with an Improvement from Baseline in Cutaneous Lupus Erythematosus Area and Severity Index (CLASI) Activity Score ≥ 50% at Week 8, 12, 24, 36, and 52 in Participants with a CLASI Activity Score ≥ 8 at Baseline

End point title	Number of Participants with an Improvement from Baseline in Cutaneous Lupus Erythematosus Area and Severity Index (CLASI) Activity Score ≥ 50% at Week 8, 12, 24, 36, and 52 in Participants with a CLASI Activity Score ≥ 8 at Baseline

End point description:

The CLASI consists of 2 scores, the first summarizes the activity of the disease while the second is a measure of the damage done by the disease. Activity is scored based on erythema, scale/hyperkeratosis, mucous membrane involvement, acute hair loss and non-scarring alopecia. The total score ranges from 0-70, with higher scores indicating more severe disease.

Full Analysis Set: Included all participants randomized in the study. Only participants who had a CLASI activity score ≥ 8 at baseline and the opportunity to complete the visit by the date of the study termination decision being communicated to sites were included.

End point type	Secondary

End point timeframe:

Weeks 8, 12, 24, 36 and 52

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18[26]	8[27]	14[28]	17[29]
Units: participants				
Week 8	2	1	5	9
Week 12	6	2	5	7
Week 24	4	4	5	6
Week 36	5	5	4	5
Week 52	3	0	3	3

Notes:

[26] - Week 12 N = 18
Week 24 N = 16
Week 36 N = 11
Week 52 N = 6

[27] - Week 12 N = 8
Week 24 N = 8
Week 36 N = 8
Week 52 N = 4
[28] - Week 12 N = 12
Week 24 N = 12
Week 36 N = 10
Week 52 N = 9
[29] - Week 12 N = 17
Week 24 N = 12
Week 36 N = 8
Week 52 N = 6

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Flare Rate Over 52 Weeks

End point title	Annualized Flare Rate Over 52 Weeks

End point description:

A flare was defined as a BILAG score designation of "worse" or "new" resulting in a B score in ≥ 2 organs or an A score in ≥ 1 organ. The BILAG index evaluates disease activity in 9 separate organ systems. Each of the organ systems are allocated an alphabetical score of A (most active), B (moderate activity), C (minor activity), D (stable) or E (never present).

The annualized flare rate was calculated as the number of flares divided by the flare exposure time.

Full Analysis Set: Included all participants randomized in the study.

End point type	Secondary

End point timeframe:

Up to 52 weeks

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	35	34	58
Units: Ratio				
number (not applicable)	0.3	0.5	0.7	0.4

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Fatigue Standardized Score Using the Patient-Reported Outcome Measurement Information System (PROMIS) Fatigue Short Form (SF) 7a Instrument at Week 12, 24, 36 and 52

End point title	Change from Baseline in Fatigue Standardized Score Using the Patient-Reported Outcome Measurement Information System (PROMIS) Fatigue Short Form (SF) 7a Instrument at Week 12, 24, 36 and 52

End point description:

The PROMIS Fatigue SF 7a assesses the experience of fatigue as well as its impact on physical, mental and social activities. The score ranges from 7 to 35, with higher scores indicating more fatigue. A

negative change from baseline indicates a reduction in fatigue.

Efficacy data collected after the study termination decision date were censored and excluded from analyses for that particular visit.

Full Analysis Set: Included all participants randomized in the study and had observed data.

End point type	Secondary

End point timeframe:

Baseline to Week 12, 24, 36 and 52

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37[30]	27[31]	24[32]	46[33]
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12	-4.12 (± 7.91)	-5.52 (± 5.04)	-5.78 (± 8.39)	-4.74 (± 9.60)
Week 24	-5.24 (± 8.05)	-4.95 (± 8.72)	-4.62 (± 8.03)	-7.17 (± 7.01)
Week 36	-3.20 (± 10.70)	-5.77 (± 7.09)	-5.32 (± 8.90)	-5.34 (± 10.61)
Week 52	-3.29 (± 7.64)	-8.44 (± 4.21)	-6.97 (± 14.20)	-5.47 (± 13.97)

Notes:

[30] - Week 24 N = 32
Week 36 N = 23
Week 52 N = 8
[31] - Week 24 N = 24
Week 36 N = 21
Week 52 N = 7
[32] - Week 24 N = 22
Week 36 N = 14
Week 52 N = 11
[33] - Week 24 N = 23
Week 36 N = 19
Week 52 N = 10

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Physical Component Score of the Medical Outcomes Short Form-36 Questionnaire Version 2 (SF-36V2) at Week 12, 24, 36 and 52

End point title	Change from Baseline in the Physical Component Score of the Medical Outcomes Short Form-36 Questionnaire Version 2 (SF-36V2) at Week 12, 24, 36 and 52

End point description:

The SF-36v2 contains 36 items and yields assessments of 8 domains of health-related quality of life:
1) Limitations in physical activities because of health problems
2) Limitations in social activities because of physical or emotional problems
3) Limitations in usual role activities because of physical health problems
4) Bodily pain
5) General mental health (psychological distress and well-being)
6) Limitations in usual role activities because of emotional problems
7) Vitality (energy and fatigue)
8) General health perceptions

The scores from the 8 domains will be evaluated independently and aggregated into 2 norm-based summary component measures of physical and mental health. The recall period is the past 7 days. The score ranges from 0-100 for the summary components and for each domain, with higher scores indicating better outcomes. A positive change from baseline indicates an improvement in outcomes.

Full Analysis Set: All randomized participants with observed data.

End point type	Secondary

End point timeframe:

Baseline to Week 12, 24, 36 and 52

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37[34]	27[35]	24[36]	46[37]
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12	4.349 (± 7.526)	6.016 (± 7.854)	6.450 (± 6.701)	2.615 (± 7.622)
Week 24	6.709 (± 7.520)	5.544 (± 7.624)	4.726 (± 7.058)	5.136 (± 8.351)
Week 36	5.391 (± 9.040)	6.576 (± 6.331)	7.524 (± 8.988)	3.648 (± 8.269)
Week 52	3.678 (± 2.958)	6.206 (± 4.144)	8.724 (± 9.159)	6.252 (± 12.226)

Notes:

[34] - Week 24 N = 32
Week 36 N = 23
Week 52 N = 8
[35] - Week 24 N = 24
Week 36 N = 21
Week 52 N = 7
[36] - Week 24 N = 22
Week 36 N = 14
Week 52 N = 11
[37] - Week 24 N = 33
Week 36 N = 19
Week 52 N = 10

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Mental Component Score of the SF-36V2 at Week 12, 24, 36 and 52

End point title	Change from Baseline in the Mental Component Score of the SF-36V2 at Week 12, 24, 36 and 52

End point description:

The SF-36v2 contains 36 items and yields assessments of 8 domains of health-related quality of life:
1) Limitations in physical activities because of health problems
2) Limitations in social activities because of physical or emotional problems
3) Limitations in usual role activities because of physical health problems
4) Bodily pain
5) General mental health (psychological distress and well-being)
6) Limitations in usual role activities because of emotional problems
7) Vitality (energy and fatigue)
8) General health perceptions

The scores from the 8 domains will be evaluated independently and aggregated into 2 norm-based summary component measures of physical and mental health. The recall period is the past 7 days. The score ranges from 0-100 for the summary components and for each domain, with higher scores indicating better outcomes. A positive change from baseline indicates an improvement in outcomes.

Full Analysis Set: All randomized participants with observed data.

End point type	Secondary

End point timeframe:

Baseline to Week 12, 24, 36 and 52

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37[38]	27[39]	24[40]	46[41]
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12	5.079 (± 11.395)	0.080 (± 10.789)	3.087 (± 11.651)	1.867 (± 9.092)
Week 24	6.510 (± 12.498)	0.498 (± 10.902)	1.585 (± 9.032)	3.959 (± 9.220)
Week 36	5.587 (± 14.482)	-0.118 (± 10.560)	3.129 (± 12.141)	0.564 (± 13.586)
Week 52	4.781 (± 8.485)	1.106 (± 9.633)	-1.813 (± 16.608)	-2.163 (± 13.023)

Notes:

[38] - Week 24 N = 32
Week 36 N = 23
Week 52 N = 8
[39] - Week 24 N = 24
Week 36 N = 21
Week 52 N = 7
[40] - Week 24 N = 22
Week 36 N = 14
Week 52 N = 11
[41] - Week 24 N = 33
Week 36 N = 19
Week 52 N = 10

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Physical Functioning Domain Score of the SF-36V2 at Week 12, 24, 36 and 52

End point title	Change from Baseline in the Physical Functioning Domain Score of the SF-36V2 at Week 12, 24, 36 and 52

End point description:

The SF-36v2 contains 36 items and yields assessments of 8 domains of health-related quality of life:
1) Limitations in physical activities because of health problems
2) Limitations in social activities because of physical or emotional problems
3) Limitations in usual role activities because of physical health problems
4) Bodily pain
5) General mental health (psychological distress and well-being)
6) Limitations in usual role activities because of emotional problems
7) Vitality (energy and fatigue)
8) General health perceptions

The scores from the 8 domains will be evaluated independently and aggregated into 2 norm-based summary component measures of physical and mental health. The recall period is the past 7 days. The score ranges from 0-100 for the summary components and for each domain, with higher scores indicating better outcomes. A positive change from baseline indicates an improvement in outcomes.

Full Analysis Set: All randomized participants with observed data.

End point type	Secondary

End point timeframe:

Baseline to Week 12, 24, 36 and 52

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37[42]	27[43]	24[44]	46[45]
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12	14.460 (± 21.532)	7.963 (± 15.888)	14.165 (± 22.489)	5.761 (± 22.034)
Week 24	20.469 (± 23.048)	6.876 (± 20.998)	14.545 (± 21.816)	10.607 (± 24.036)
Week 36	13.477 (± 26.261)	10.713 (± 20.078)	16.786 (± 29.910)	9.736 (± 29.603)
Week 52	8.750 (± 14.083)	15.714 (± 13.973)	18.183 (± 28.919)	15.001 (± 31.622)

Notes:

[42] - Week 24 N = 32
Week 36 N = 23
Week 52 N = 8
[43] - Week 24 N = 24
Week 36 N = 21
Week 52 N = 7
[44] - Week 24 N = 22
Week 36 N = 14
Week 52 N = 11
[45] - Week 24 N = 33
Week 36 N = 19
Week 52 N = 10

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Social Role Functioning Domain Score of the SF-36V2 at Week 12, 24, 36 and 52

End point title	Change from Baseline in the Social Role Functioning Domain Score of the SF-36V2 at Week 12, 24, 36 and 52

End point description:

The SF-36v2 contains 36 items and yields assessments of 8 domains of health-related quality of life:
1) Limitations in physical activities because of health problems
2) Limitations in social activities because of physical or emotional problems
3) Limitations in usual role activities because of physical health problems
4) Bodily pain
5) General mental health (psychological distress and well-being)
6) Limitations in usual role activities because of emotional problems
7) Vitality (energy and fatigue)
8) General health perceptions

The scores from the 8 domains will be evaluated independently and aggregated into 2 norm-based summary component measures of physical and mental health. The recall period is the past 7 days. The score ranges from 0-100 for the summary components and for each domain, with higher scores indicating better outcomes. A positive change from baseline indicates an improvement in outcomes.

Full Analysis Set: All randomized participants with observed data.

End point type	Secondary

End point timeframe:

Baseline to Week 12, 24, 36 and 52

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37[46]	27[47]	24[48]	46[49]
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12	15.54 (± 29.82)	9.72 (± 22.29)	7.81 (± 26.79)	2.17 (± 21.46)
Week 24	21.88 (± 33.15)	13.02 (± 23.16)	3.98 (± 24.52)	9.47 (± 25.39)
Week 36	13.04 (± 38.71)	8.93 (± 26.26)	16.96 (± 32.75)	1.32 (± 29.14)
Week 52	10.94 (± 28.69)	21.43 (± 20.04)	5.68 (± 35.95)	-1.25 (± 36.54)

Notes:

[46] - Week 24 N = 32
Week 36 N = 23
Week 52 N = 8
[47] - Week 24 N = 24
Week 36 N = 21
Week 52 N = 7
[48] - Week 24 N = 22
Week 36 N = 14
Week 52 N = 11
[49] - Week 24 N = 33
Week 36 N = 19
Week 52 N = 10

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Physical Role Functioning Domain Score of the SF-36V2 at Week 12, 24, 36 and 52

End point title	Change from Baseline in the Physical Role Functioning Domain Score of the SF-36V2 at Week 12, 24, 36 and 52

End point description:

The SF-36v2 contains 36 items and yields assessments of 8 domains of health-related quality of life:
1) Limitations in physical activities because of health problems
2) Limitations in social activities because of physical or emotional problems
3) Limitations in usual role activities because of physical health problems
4) Bodily pain
5) General mental health (psychological distress and well-being)
6) Limitations in usual role activities because of emotional problems
7) Vitality (energy and fatigue)
8) General health perceptions

The scores from the 8 domains will be evaluated independently and aggregated into 2 norm-based summary component measures of physical and mental health. The recall period is the past 7 days. The score ranges from 0-100 for the summary components and for each domain, with higher scores indicating better outcomes. A positive change from baseline indicates an improvement in outcomes.

Full Analysis Set: All randomized participants with observed data.

End point type	Secondary

End point timeframe:

Baseline to Week 12, 24, 36 and 52

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37[50]	27[51]	24[52]	46[53]
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12	12.838 (± 24.516)	15.509 (± 26.081)	13.802 (± 22.571)	6.929 (± 21.899)
Week 24	18.359 (± 22.221)	14.323 (± 26.290)	9.091 (± 20.479)	15.909 (± 23.804)
Week 36	11.685 (± 26.935)	14.881 (± 26.917)	15.179 (± 24.966)	7.895 (± 29.377)
Week 52	11.719 (± 15.468)	18.750 (± 14.878)	19.318 (± 25.381)	6.875 (± 35.041)

Notes:

[50] - Week 24 N = 32
Week 36 N = 23
Week 52 N = 8
[51] - Week 24 N = 24
Week 36 N = 21
Week 52 N = 7
[52] - Week 24 N = 22
Week 36 N = 14
Week 52 N = 11
[53] - Week 24 N = 33
Week 36 N = 19
Week 52 N = 10

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Bodily Pain Domain Score of the SF-36V2 at Week 12, 24, 36 and 52

End point title	Change from Baseline in the Bodily Pain Domain Score of the SF-36V2 at Week 12, 24, 36 and 52

End point description:

The SF-36v2 contains 36 items and yields assessments of 8 domains of health-related quality of life:
1) Limitations in physical activities because of health problems
2) Limitations in social activities because of physical or emotional problems
3) Limitations in usual role activities because of physical health problems
4) Bodily pain
5) General mental health (psychological distress and well-being)
6) Limitations in usual role activities because of emotional problems
7) Vitality (energy and fatigue)
8) General health perceptions

The scores from the 8 domains will be evaluated independently and aggregated into 2 norm-based summary component measures of physical and mental health. The recall period is the past 7 days. The score ranges from 0-100 for the summary components and for each domain, with higher scores indicating better outcomes. A positive change from baseline indicates an improvement in outcomes.

Full Analysis Set: All randomized participants with observed data.

End point type	Secondary

End point timeframe:

Baseline to Week 12, 24, 36 and 52

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37[54]	27[55]	24[56]	46[57]
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12	13.6 (± 25.1)	13.7 (± 23.0)	18.8 (± 22.6)	10.2 (± 23.0)
Week 24	20.4 (± 26.6)	14.3 (± 21.5)	13.8 (± 23.1)	18.4 (± 26.6)
Week 36	22.0 (± 26.3)	19.5 (± 20.7)	24.6 (± 33.0)	15.4 (± 23.3)
Week 52	10.4 (± 7.7)	11.1 (± 17.1)	17.9 (± 29.7)	16.7 (± 37.1)

Notes:

[54] - Week 24 N = 32
Week 36 N = 23
Week 52 N = 8
[55] - Week 24 N = 24
Week 36 N = 21
Week 52 N = 7
[56] - Week 24 N = 22
Week 36 N = 14
Week 52 N = 11
[57] - Week 24 N = 33
Week 36 N = 19
Week 52 N = 10

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Mental Health Domain Score of the SF-36V2 at Week 12, 24, 36 and 52

End point title	Change from Baseline in the Mental Health Domain Score of the SF-36V2 at Week 12, 24, 36 and 52

End point description:

The SF-36v2 contains 36 items and yields assessments of 8 domains of health-related quality of life:
1) Limitations in physical activities because of health problems
2) Limitations in social activities because of physical or emotional problems
3) Limitations in usual role activities because of physical health problems
4) Bodily pain
5) General mental health (psychological distress and well-being)
6) Limitations in usual role activities because of emotional problems
7) Vitality (energy and fatigue)
8) General health perceptions

The scores from the 8 domains will be evaluated independently and aggregated into 2 norm-based summary component measures of physical and mental health. The recall period is the past 7 days. The score ranges from 0-100 for the summary components and for each domain, with higher scores indicating better outcomes. A positive change from baseline indicates an improvement in outcomes.

Full Analysis Set: All randomized participants with observed data.

End point type	Secondary

End point timeframe:

Baseline to Week 12, 24, 36 and 52

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37[58]	27[59]	24[60]	46[61]
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12	8.2 (± 19.3)	1.3 (± 18.7)	9.4 (± 22.5)	5.2 (± 17.4)
Week 24	12.0 (± 21.2)	3.8 (± 22.4)	7.5 (± 19.6)	9.4 (± 17.8)
Week 36	9.6 (± 23.2)	-1.9 (± 18.4)	6.4 (± 22.6)	6.6 (± 24.3)
Week 52	7.5 (± 16.7)	-2.1 (± 22.7)	0.5 (± 33.0)	1.5 (± 28.5)

Notes:

[58] - Week 24 N = 32
Week 36 N = 23
Week 52 N = 8
[59] - Week 24 N = 24
Week 36 N = 21
Week 52 N = 7
[60] - Week 24 N = 22
Week 36 N = 14
Week 52 N = 11
[61] - Week 24 N = 33
Week 36 N = 19
Week 52 N = 10

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Emotional Role Domain Score of the SF-36V2 at Week 12, 24, 36 and 52

End point title	Change from Baseline in the Emotional Role Domain Score of the SF-36V2 at Week 12, 24, 36 and 52

End point description:

The SF-36v2 contains 36 items and yields assessments of 8 domains of health-related quality of life:
1) Limitations in physical activities because of health problems
2) Limitations in social activities because of physical or emotional problems
3) Limitations in usual role activities because of physical health problems
4) Bodily pain
5) General mental health (psychological distress and well-being)
6) Limitations in usual role activities because of emotional problems
7) Vitality (energy and fatigue)
8) General health perceptions

The scores from the 8 domains will be evaluated independently and aggregated into 2 norm-based summary component measures of physical and mental health. The recall period is the past 7 days. The score ranges from 0-100 for the summary components and for each domain, with higher scores indicating better outcomes. A positive change from baseline indicates an improvement in outcomes.

Full Analysis Set: All randomized participants with observed data.

End point type	Secondary

End point timeframe:

Baseline to Week 12, 24, 36 and 52

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37[62]	27[63]	24[64]	46[65]
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12	13.964 (± 27.781)	-3.704 (± 23.036)	4.514 (± 26.236)	3.804 (± 23.812)
Week 24	16.926 (± 29.820)	-5.208 (± 23.417)	3.031 (± 23.223)	8.333 (± 25.769)
Week 36	17.028 (± 35.129)	5.952 (± 24.029)	6.548 (± 29.810)	-0.440 (± 33.847)
Week 52	9.375 (± 18.057)	8.334 (± 14.433)	-2.273 (± 33.144)	-9.168 (± 32.972)

Notes:

[62] - Week 24 N = 32
Week 36 N = 23
Week 52 N = 8
[63] - Week 24 N = 24
Week 36 N = 21
Week 52 N = 7
[64] - Week 24 N = 22
Week 36 N = 14
Week 52 N = 11
[65] - Week 24 N = 33
Week 36 N = 19
Week 52 N = 10

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Vitality Domain Score of the SF-36V2 at Week 12, 24, 36 and 52

End point title	Change from Baseline in the Vitality Domain Score of the SF-36V2 at Week 12, 24, 36 and 52

End point description:

The SF-36v2 contains 36 items and yields assessments of 8 domains of health-related quality of life:
1) Limitations in physical activities because of health problems
2) Limitations in social activities because of physical or emotional problems
3) Limitations in usual role activities because of physical health problems
4) Bodily pain
5) General mental health (psychological distress and well-being)
6) Limitations in usual role activities because of emotional problems
7) Vitality (energy and fatigue)
8) General health perceptions

The scores from the 8 domains will be evaluated independently and aggregated into 2 norm-based summary component measures of physical and mental health. The recall period is the past 7 days. The score ranges from 0-100 for the summary components and for each domain, with higher scores indicating better outcomes. A positive change from baseline indicates an improvement in outcomes.

Full Analysis Set: All randomized participants with observed data.

End point type	Secondary

End point timeframe:

Baseline to Week 12, 24, 36 and 52

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37[66]	27[67]	24[68]	46[69]
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12	10.642 (± 20.405)	12.037 (± 21.225)	15.365 (± 23.384)	7.609 (± 20.536)
Week 24	13.477 (± 23.283)	8.333 (± 23.936)	8.523 (± 20.912)	12.879 (± 19.884)
Week 36	11.685 (± 26.935)	6.548 (± 19.811)	14.732 (± 23.718)	5.592 (± 22.812)
Week 52	15.625 (± 19.480)	4.464 (± 22.160)	9.659 (± 28.141)	13.750 (± 26.484)

Notes:

[66] - Week 24 N = 32
Week 36 N = 23
Week 52 N = 8
[67] - Week 24 N = 24
Week 36 N = 21
Week 52 N = 7
[68] - Week 24 N = 22
Week 36 N = 14
Week 52 N = 11
[69] - Week 24 N = 33
Week 36 N = 19
Week 52 N = 10

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the General Health Domain Score of the SF-36V2 at Week 12, 24, 36 and 52

End point title	Change from Baseline in the General Health Domain Score of the SF-36V2 at Week 12, 24, 36 and 52

End point description:

The SF-36v2 contains 36 items and yields assessments of 8 domains of health-related quality of life:
1) Limitations in physical activities because of health problems
2) Limitations in social activities because of physical or emotional problems
3) Limitations in usual role activities because of physical health problems
4) Bodily pain
5) General mental health (psychological distress and well-being)
6) Limitations in usual role activities because of emotional problems
7) Vitality (energy and fatigue)
8) General health perceptions

The scores from the 8 domains will be evaluated independently and aggregated into 2 norm-based summary component measures of physical and mental health. The recall period is the past 7 days. The score ranges from 0-100 for the summary components and for each domain, with higher scores indicating better outcomes. A positive change from baseline indicates an improvement in outcomes.

Full Analysis Set: All randomized participants with observed data.

End point type	Secondary

End point timeframe:

Baseline to Week 12, 24, 36 and 52

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37[70]	27[71]	24[72]	46[73]
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12	5.2 (± 15.8)	6.1 (± 17.7)	10.6 (± 15.9)	2.6 (± 16.2)
Week 24	9.2 (± 17.7)	6.2 (± 19.0)	3.8 (± 16.2)	5.6 (± 15.3)
Week 36	10.7 (± 16.1)	5.6 (± 14.9)	7.2 (± 17.2)	-2.1 (± 16.6)
Week 52	7.5 (± 8.9)	2.4 (± 5.9)	6.7 (± 19.0)	0.5 (± 29.5)

Notes:

[70] - Week 24 N = 32
Week 36 N = 23
Week 52 N = 8
[71] - Week 24 N = 24
Week 36 N = 21
Week 52 N = 7
[72] - Week 24 N = 22
Week 36 N = 14
Week 52 N = 11
[73] - Week 24 N = 33
Week 36 N = 19
Week 52 N = 10

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Physical Health Domain Score of the Lupus Quality of Life (LupusQoL) at Week 12, 24, 36 and 52

End point title	Change from Baseline in the Physical Health Domain Score of the Lupus Quality of Life (LupusQoL) at Week 12, 24, 36 and 52

End point description:

The LupusQoL is a systemic lupus erythematosus (SLE)-specific health-related QoL instrument and consists of 8 domains:
1) Physical health.
2) Pain.
3) Planning.
4) Intimate relationships.
5) Burden to others.
6) Emotional health.
7) Body image.
8) Fatigue.

The score for each domain ranges from 0-100, with higher scores indicating better outcomes. A positive change from baseline indicates an improvement in outcomes.

Full Analysis Set: Included all participants randomized in the study and had observed data.

End point type	Secondary

End point timeframe:

Baseline to Week 12, 24, 36 and 52

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34[74]	26[75]	22[76]	42[77]
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12	13.7868 (± 20.5586)	12.6202 (± 18.9259)	13.7784 (± 18.3909)	11.5327 (± 22.3595)
Week 24	15.5172 (± 23.7770)	9.5109 (± 25.1501)	15.4688 (± 17.7205)	13.8542 (± 25.3834)
Week 36	11.3636 (± 20.6738)	13.4375 (± 20.2549)	18.7500 (± 24.4404)	5.7292 (± 24.3304)
Week 52	9.3750 (± 11.8114)	20.8333 (± 21.1640)	15.6250 (± 27.0994)	10.6250 (± 29.5437)

Notes:

[74] - Week 24 N = 29
Week 36 N = 22
Week 52 N = 8
[75] - Week 24 N = 23
Week 36 N = 20
Week 52 N = 6
[76] - Week 24 N = 20
Week 36 N = 13
Week 52 N = 11
[77] - Week 24 N = 30
Week 36 N = 18
Week 52 N = 10

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Pain Domain Score of the LupusQoL at Week 12, 24, 36 and 52

End point title	Change from Baseline in the Pain Domain Score of the LupusQoL at Week 12, 24, 36 and 52

End point description:

The LupusQoL is a SLE-specific health-related QoL instrument and consists of 8 domains:
1) Physical health.
2) Pain.
3) Planning.
4) Intimate relationships.
5) Burden to others.
6) Emotional health.
7) Body image.
8) Fatigue.

The score for each domain ranges from 0-100, with higher scores indicating better outcomes. A positive change from baseline indicates an improvement in outcomes.

Full Analysis Set: Included all participants randomized in the study and had observed data.

End point type	Secondary

End point timeframe:

Baseline to Week 12, 24, 36 and 52

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34[78]	25[79]	22[80]	42[81]
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12	17.892 (± 22.392)	16.333 (± 23.873)	17.424 (± 23.975)	13.294 (± 24.072)
Week 24	21.264 (± 28.311)	14.773 (± 25.708)	11.667 (± 23.939)	11.944 (± 28.339)
Week 36	12.879 (± 25.423)	17.105 (± 21.956)	16.667 (± 30.238)	5.556 (± 28.296)
Week 52	14.583 (± 18.767)	16.667 (± 8.333)	8.333 (± 27.639)	11.667 (± 27.833)

Notes:

[78] - Week 24 N = 29
Week 36 N = 22
Week 52 N = 8
[79] - Week 24 N = 22
Week 36 N = 19
Week 52 N = 5
[80] - Week 24 N = 20
Week 36 N = 13
Week 52 N = 11
[81] - Week 24 N = 30
Week 36 N = 18
Week 52 N = 10

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Planning Domain Score of the LupusQoL at Week 12, 24, 36 and 52

End point title	Change from Baseline in the Planning Domain Score of the LupusQoL at Week 12, 24, 36 and 52

End point description:

The LupusQoL is a SLE-specific health-related QoL instrument and consists of 8 domains:
1) Physical health.
2) Pain.
3) Planning.
4) Intimate relationships.
5) Burden to others.
6) Emotional health.
7) Body image.
8) Fatigue.

The score for each domain ranges from 0-100, with higher scores indicating better outcomes. A positive change from baseline indicates an improvement in outcomes.

Full Analysis Set: Included all participants randomized in the study and had observed data.

End point type	Secondary

End point timeframe:

Baseline to Week 12, 24, 36 and 52

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34[82]	25[83]	22[84]	42[85]
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12	9.804 (± 23.071)	17.000 (± 23.259)	13.636 (± 23.925)	7.143 (± 23.825)
Week 24	11.494 (± 29.915)	14.015 (± 28.334)	15.833 (± 22.926)	14.722 (± 22.391)
Week 36	12.500 (± 30.834)	9.211 (± 23.553)	13.462 (± 23.457)	5.093 (± 29.861)
Week 52	15.625 (± 29.693)	15.000 (± 18.066)	10.606 (± 25.025)	12.500 (± 27.287)

Notes:

[82] - Week 24 N = 29
Week 36 N = 22
Week 52 N = 8
[83] - Week 24 N = 22
Week 36 N = 19
Week 52 N = 5
[84] - Week 24 N = 20
Week 36 N = 13
Week 52 N = 11
[85] - Week 24 N = 30
Week 36 N = 18
Week 52 N = 10

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Burden to Others Domain Score of the LupusQoL at Week 12, 24, 36 and 52

End point title	Change from Baseline in the Burden to Others Domain Score of the LupusQoL at Week 12, 24, 36 and 52

End point description:

The LupusQoL is a SLE-specific health-related QoL instrument and consists of 8 domains:
1) Physical health.
2) Pain.
3) Planning.
4) Intimate relationships.
5) Burden to others.
6) Emotional health.
7) Body image.
8) Fatigue.

The score for each domain ranges from 0-100, with higher scores indicating better outcomes. A positive change from baseline indicates an improvement in outcomes.

Full Analysis Set: Included all participants randomized in the study and had observed data.

End point type	Secondary

End point timeframe:

Baseline to Week 12, 24, 36 and 52

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34[86]	25[87]	22[88]	42[89]
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12	10.784 (± 28.169)	14.333 (± 17.099)	17.803 (± 30.134)	6.944 (± 29.673)
Week 24	20.115 (± 31.459)	5.682 (± 24.719)	12.083 (± 23.798)	12.778 (± 29.093)
Week 36	14.773 (± 30.530)	10.088 (± 22.149)	21.795 (± 22.448)	18.519 (± 26.438)
Week 52	16.667 (± 22.713)	38.333 (± 19.185)	21.212 (± 23.677)	18.333 (± 28.273)

Notes:

[86] - Week 24 N = 29
Week 36 N = 22
Week 52 N = 8
[87] - Week 24 N = 22
Week 36 N = 19
Week 52 N = 5
[88] - Week 24 N = 20
Week 36 N = 13
Week 52 N = 11
[89] - Week 24 N = 30
Week 36 N = 18
Week 52 N = 10

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Intimate Relationship Domain Score of the LupusQoL at Week 12, 24, 36 and 52

End point title	Change from Baseline in the Intimate Relationship Domain Score of the LupusQoL at Week 12, 24, 36 and 52

End point description:

The LupusQoL is a SLE-specific health-related QoL instrument and consists of 8 domains:
1) Physical health.
2) Pain.
3) Planning.
4) Intimate relationships.
5) Burden to others.
6) Emotional health.
7) Body image.
8) Fatigue.

The score for each domain ranges from 0-100, with higher scores indicating better outcomes. A positive change from baseline indicates an improvement in outcomes.

Full Analysis Set: Included all participants randomized in the study and had observed data.

End point type	Secondary

End point timeframe:

Baseline to Week 12, 24, 36 and 52

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21[90]	18[91]	16[92]	29[93]
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12	17.26 (± 27.52)	3.47 (± 22.61)	14.29 (± 35.65)	11.21 (± 31.04)
Week 24	10.83 (± 35.00)	1.56 (± 26.57)	19.53 (± 28.86)	13.16 (± 29.01)
Week 36	10.94 (± 33.81)	-1.67 (± 30.20)	11.36 (± 30.34)	12.50 (± 15.99)
Week 52	6.25 (± 51.08)	0.00 (± 8.84)	9.38 (± 35.83)	8.33 (± 31.29)

Notes:

[90] - Week 24 N = 15
Week 36 N = 16
Week 52 N = 6
[91] - Week 24 N = 16
Week 36 N = 15
Week 52 N = 5
[92] - Week 24 N = 16
Week 36 N = 11
Week 52 N = 8
[93] - Week 24 N = 19
Week 36 N = 12
Week 52 N = 6

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Emotional Health Domain Score of the LupusQoL at Week 12, 24, 36 and 52

End point title	Change from Baseline in the Emotional Health Domain Score of the LupusQoL at Week 12, 24, 36 and 52

End point description:

The LupusQoL is a SLE-specific health-related QoL instrument and consists of 8 domains:
1) Physical health.
2) Pain.
3) Planning.
4) Intimate relationships.
5) Burden to others.
6) Emotional health.
7) Body image.
8) Fatigue.

The score for each domain ranges from 0-100, with higher scores indicating better outcomes. A positive change from baseline indicates an improvement in outcomes.

Full Analysis Set: Included all participants randomized in the study and had observed data.

End point type	Secondary

End point timeframe:

Baseline to Week 12, 24, 36 and 52

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34[94]	25[95]	22[96]	42[97]
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12	9.681 (± 21.729)	10.667 (± 19.021)	14.962 (± 28.425)	5.258 (± 21.465)
Week 24	13.218 (± 26.495)	7.765 (± 19.974)	11.458 (± 20.894)	9.722 (± 21.283)
Week 36	10.038 (± 25.994)	6.798 (± 18.799)	20.192 (± 24.641)	3.704 (± 30.178)
Week 52	4.167 (± 20.534)	13.333 (± 21.123)	15.530 (± 27.518)	-5.000 (± 25.595)

Notes:

[94] - Week 24 N = 29
Week 36 N = 22
Week 52 N = 8
[95] - Week 24 N = 22
Week 36 N = 19
Week 52 N = 5
[96] - Week 24 N = 20
Week 36 N = 13
Week 52 N = 11
[97] - Week 24 N = 30
Week 36 N = 18
Week 52 N = 10

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Body Image Domain Score of the LupusQoL at Week 12, 24, 36 and 52

End point title	Change from Baseline in the Body Image Domain Score of the LupusQoL at Week 12, 24, 36 and 52

End point description:

The LupusQoL is a SLE-specific health-related QoL instrument and consists of 8 domains:
1) Physical health.
2) Pain.
3) Planning.
4) Intimate relationships.
5) Burden to others.
6) Emotional health.
7) Body image.
8) Fatigue.

The score for each domain ranges from 0-100, with higher scores indicating better outcomes. A positive change from baseline indicates an improvement in outcomes.

Full Analysis Set: Included all participants randomized in the study and had observed data.

End point type	Secondary

End point timeframe:

Baseline to Week 12, 24, 36 and 52

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34[98]	25[99]	22[100]	42[101]
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12	9.6 (± 26.5)	9.0 (± 18.7)	4.1 (± 34.0)	4.6 (± 26.6)
Week 24	11.6 (± 30.6)	2.3 (± 25.5)	3.0 (± 28.2)	5.2 (± 29.6)
Week 36	6.1 (± 25.6)	14.7 (± 21.4)	18.8 (± 41.2)	6.1 (± 28.0)
Week 52	12.5 (± 33.3)	17.0 (± 22.5)	7.7 (± 37.4)	5.5 (± 36.6)

Notes:

[98] - Week 24 N = 29
Week 36 N = 22
Week 52 N = 8
[99] - Week 24 N = 22
Week 36 N = 19
Week 52 N = 5
[100] - Week 24 N = 20
Week 36 N = 13
Week 52 N = 11
[101] - Week 24 N = 30
Week 36 N = 18
Week 52 N = 10

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Fatigue Domain Score of the LupusQoL at Week 12, 24, 36 and 52

End point title	Change from Baseline in the Fatigue Domain Score of the LupusQoL at Week 12, 24, 36 and 52

End point description:

The LupusQoL is a SLE-specific health-related QoL instrument and consists of 8 domains:
1) Physical health.
2) Pain.
3) Planning.
4) Intimate relationships.
5) Burden to others.
6) Emotional health.
7) Body image.
8) Fatigue.

The score for each domain ranges from 0-100, with higher scores indicating better outcomes. A positive change from baseline indicates an improvement in outcomes.

Full Analysis Set: Included all participants randomized in the study and had observed data.

End point type	Secondary

End point timeframe:

Baseline to Week 12, 24, 36 and 52

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34[102]	25[103]	22[104]	42[105]
Units: score on a scale				
arithmetic mean (standard deviation)				
Week 12	8.456 (± 23.329)	9.750 (± 15.104)	15.909 (± 21.368)	8.185 (± 21.273)
Week 24	10.776 (± 24.600)	7.670 (± 23.059)	13.750 (± 20.135)	13.542 (± 20.108)
Week 36	5.966 (± 29.345)	10.526 (± 17.561)	12.019 (± 26.695)	4.514 (± 23.853)
Week 52	10.938 (± 15.580)	25.000 (± 4.419)	15.341 (± 26.274)	16.250 (± 28.596)

Notes:

[102] - Week 24 N = 29
Week 36 N = 22
Week 52 N = 8

[103] - Week 24 N = 22
Week 36 N = 19
Week 52 N = 5

[104] - Week 24 N = 20
Week 36 N = 13
Week 52 N = 11

[105] - Week 24 N = 30
Week 36 N = 18
Week 52 N = 10

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Efavaleukin Alfa Concentrations by Timepoint

End point title	Serum Efavaleukin Alfa Concentrations by Timepoint[106]

End point description:

Serum efavaleukin alfa concentrations by timepoint after multiple dose subcutaneous administration of efavaleukin alfa to participants with active systemic lupus erythematosus. Lower limit of quantification= 0.100 ng/mL.

The PK Concentration Analysis Set is defined as the subset of participants in the Safety Analysis Set who had at least 1 evaluable serum concentration (including results below the level of detection) of investigational product. PK concentration data will be analyzed according to the actual treatment received.

End point type	Secondary

End point timeframe:

Day 1: 6-24 and 48-96 hrs, Day 29, Day 43: 6-24 and 48-96 hrs, Day 85, Day 169, Day 253, Day 309, and Day 365

Notes:

[106] - 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: Endpoint is only applicable to participants receiving Efavaleukin Alfa.

End point values	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	34	30	53	
Units: ng/mL				
arithmetic mean (standard error)				
Day 1: 6-24 hrs n= 34, 29, 53	5.46 (± 5.18)	12.8 (± 12.3)	27.4 (± 25.7)	
Day 1: 48-96 hrs n= 34, 30, 49	2.34 (± 2.52)	5.93 (± 6.45)	21.8 (± 30.5)	
Day 29 n= 26, 24, 39	0.0201 (± 0.0649)	0.0179 (± 0.0496)	0.0699 (± 0.173)	
Day 43: 6-24 hrs n= 21, 21, 39	4.34 (± 5.55)	13.9 (± 11.7)	25.0 (± 22.6)	
Day 43: 48-96 hrs n= 23, 21, 41	2.80 (± 4.39)	12.7 (± 17.2)	18.1 (± 19.0)	
Day 85 n= 15, 17, 27	0.0577 (± 0.223)	0.00712 (± 0.0293)	0.191 (± 0.316)	
Day 169 n= 14, 12, 17	0.349 (± 1.10)	0.0588 (± 0.133)	0.140 (± 0.178)	
Day 253 n= 18, 7, 11	0.530 (± 1.48)	0.155 (± 0.221)	0.458 (± 0.71)	
Day 309 n= 9, 9, 3	0.252 (± 0.502)	0.0558 (± 0.167)	0.308 (± 0.533)	
Day 365 n= 5, 4, 3	0.00 (± 0.00)	0.00 (± 0.00)	0.136 (± 0.236)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Experienced a Treatment-emergent Adverse Event (TEAE)

End point title	Number of Participants Who Experienced a Treatment-emergent Adverse Event (TEAE)

End point description:

A TEAE was defined as any untoward medical occurrence irrespective of a causal relationship with the study treatment and had emerged or worsened during treatment.

A serious TEAE was defined as any untoward medical occurrence that, met at least 1 of the following criteria:
- Resulted in death (fatal).
- Was immediately life-threatening.
- Required in-patient hospitalization or prolongation of existing hospitalization.
- Resulted in persistent or significant disability/incapacity.
- Was a congenital anomaly/birth defect.
- Was any other medically important serious event.

Clinically significant changes from baseline in laboratory values and vital signs were also recorded as TEAEs.

Safety Analysis Set: All randomized participants who received at least 1 dose of investigational product. After randomization, 1 participant received more than their planned medium dose of efavaleukin alfa in error, therefore the participant is also counted in the efavaleukin alfa high dose arm.

End point type	Secondary

End point timeframe:

Day 1 to Week 56

End point values	Placebo	Efavaleukin Alfa Low Dose	Efavaleukin Alfa Medium Dose	Efavaleukin Alfa High Dose
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	35	33	58[107]
Units: participants				
TEAE	29	29	33	55
Serious TEAE	4	3	4	3

Notes:

[107] - N = 59

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality: From enrollment until the end of study; median (min, max) time on study was 38.23 (0.28, 62.93) weeks. Serious TEAEs and other TEAEs: Day 1 to Week 56.

Adverse event reporting additional description:

All-cause mortality reported for all enrolled participants. Treatment-emergent SAEs/TEAEs reported for participants who received at least one dose of study drug.

After randomization, 1 participant received more than planned medium dose of efavaleukin alfa in error, therefore the participant is also counted in the efavaleukin alfa high dose arm.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received placebo matching efavaleukin alfa Q2W through a SC injection for up to 52 weeks.

Reporting group title	Efavaleukin alfa High Dose

Reporting group description:

Participants received high dose efavaleukin alfa Q2W through a SC injection for up to 52 weeks.

Reporting group title	Efavaleukin Alfa Medium Dose

Reporting group description:

Participants received medium dose efavaleukin alfa Q2W through a SC injection for up to 52 weeks.

Reporting group title	Efavaleukin Alfa Low Dose

Reporting group description:

Participants received low dose efavaleukin alfa Q2W through a SC injection for up to 52 weeks.

Serious adverse events	Placebo	Efavaleukin alfa High Dose	Efavaleukin Alfa Medium Dose
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 41 (9.76%)	3 / 59 (5.08%)	4 / 33 (12.12%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anal squamous cell carcinoma			
subjects affected / exposed	0 / 41 (0.00%)	0 / 59 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Contusion			

subjects affected / exposed	0 / 41 (0.00%)	1 / 59 (1.69%)	0 / 33 (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			
Transient ischaemic attack			
subjects affected / exposed	1 / 41 (2.44%)	0 / 59 (0.00%)	0 / 33 (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
Stroke in evolution			
subjects affected / exposed	0 / 41 (0.00%)	1 / 59 (1.69%)	0 / 33 (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
Headache			
subjects affected / exposed	0 / 41 (0.00%)	0 / 59 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain stem infarction			
subjects affected / exposed	0 / 41 (0.00%)	1 / 59 (1.69%)	0 / 33 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 59 (0.00%)	0 / 33 (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			
Colitis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 59 (0.00%)	0 / 33 (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
Respiratory, thoracic and mediastinal disorders			
Pulmonary alveolar haemorrhage			

subjects affected / exposed	0 / 41 (0.00%)	0 / 59 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	0 / 41 (0.00%)	0 / 59 (0.00%)	1 / 33 (3.03%)
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			
Arthritis			
subjects affected / exposed	0 / 41 (0.00%)	0 / 59 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Sepsis			
subjects affected / exposed	2 / 41 (4.88%)	1 / 59 (1.69%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 41 (0.00%)	0 / 59 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 41 (0.00%)	0 / 59 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bartholin's abscess			
subjects affected / exposed	0 / 41 (0.00%)	0 / 59 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Efavaleukin Alfa Low Dose		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 35 (8.57%)		
number of deaths (all causes)	0		

number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anal squamous cell carcinoma			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Stroke in evolution			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Brain stem infarction			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Colitis			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary alveolar haemorrhage			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary hypertension			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bartholin's abscess			

subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	Efavaleukin alfa High Dose	Efavaleukin Alfa Medium Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 41 (43.90%)	48 / 59 (81.36%)	33 / 33 (100.00%)
Nervous system disorders			
Tension headache			
subjects affected / exposed	2 / 41 (4.88%)	0 / 59 (0.00%)	0 / 33 (0.00%)
occurrences (all)	2	0	0
Headache			
subjects affected / exposed	4 / 41 (9.76%)	5 / 59 (8.47%)	5 / 33 (15.15%)
occurrences (all)	5	6	9
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 41 (2.44%)	2 / 59 (3.39%)	0 / 33 (0.00%)
occurrences (all)	1	2	0
General disorders and administration site conditions			
Administration site inflammation			
subjects affected / exposed	0 / 41 (0.00%)	0 / 59 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 41 (0.00%)	0 / 59 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	0	2
Injection site discolouration			
subjects affected / exposed	0 / 41 (0.00%)	1 / 59 (1.69%)	3 / 33 (9.09%)
occurrences (all)	0	2	7
Pain			
subjects affected / exposed	1 / 41 (2.44%)	3 / 59 (5.08%)	0 / 33 (0.00%)
occurrences (all)	1	3	0
Injection site inflammation			

subjects affected / exposed	0 / 41 (0.00%)	1 / 59 (1.69%)	2 / 33 (6.06%)
occurrences (all)	0	43	23
Injection site oedema			
subjects affected / exposed	0 / 41 (0.00%)	3 / 59 (5.08%)	0 / 33 (0.00%)
occurrences (all)	0	4	0
Injection site pain			
subjects affected / exposed	1 / 41 (2.44%)	10 / 59 (16.95%)	10 / 33 (30.30%)
occurrences (all)	11	26	43
Injection site pruritus			
subjects affected / exposed	1 / 41 (2.44%)	17 / 59 (28.81%)	16 / 33 (48.48%)
occurrences (all)	2	125	146
Injection site rash			
subjects affected / exposed	0 / 41 (0.00%)	13 / 59 (22.03%)	7 / 33 (21.21%)
occurrences (all)	0	52	33
Injection site reaction			
subjects affected / exposed	0 / 41 (0.00%)	1 / 59 (1.69%)	0 / 33 (0.00%)
occurrences (all)	0	4	0
Injection site swelling			
subjects affected / exposed	0 / 41 (0.00%)	9 / 59 (15.25%)	6 / 33 (18.18%)
occurrences (all)	0	68	71
Injection site urticaria			
subjects affected / exposed	0 / 41 (0.00%)	2 / 59 (3.39%)	4 / 33 (12.12%)
occurrences (all)	0	9	6
Injection site warmth			
subjects affected / exposed	0 / 41 (0.00%)	3 / 59 (5.08%)	3 / 33 (9.09%)
occurrences (all)	0	5	13
Injection site erythema			
subjects affected / exposed	0 / 41 (0.00%)	32 / 59 (54.24%)	22 / 33 (66.67%)
occurrences (all)	0	200	234
Pyrexia			
subjects affected / exposed	1 / 41 (2.44%)	6 / 59 (10.17%)	2 / 33 (6.06%)
occurrences (all)	1	7	4
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 41 (2.44%)	2 / 59 (3.39%)	3 / 33 (9.09%)
occurrences (all)	1	2	3

Constipation			
subjects affected / exposed	2 / 41 (4.88%)	0 / 59 (0.00%)	2 / 33 (6.06%)
occurrences (all)	2	0	2
Vomiting			
subjects affected / exposed	1 / 41 (2.44%)	3 / 59 (5.08%)	2 / 33 (6.06%)
occurrences (all)	1	5	2
Nausea			
subjects affected / exposed	1 / 41 (2.44%)	2 / 59 (3.39%)	3 / 33 (9.09%)
occurrences (all)	1	2	4
Gastritis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 59 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	2 / 41 (4.88%)	2 / 59 (3.39%)	4 / 33 (12.12%)
occurrences (all)	2	2	10
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 41 (2.44%)	2 / 59 (3.39%)	1 / 33 (3.03%)
occurrences (all)	1	2	2
Urticaria			
subjects affected / exposed	1 / 41 (2.44%)	3 / 59 (5.08%)	3 / 33 (9.09%)
occurrences (all)	1	3	4
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	3 / 41 (7.32%)	0 / 59 (0.00%)	2 / 33 (6.06%)
occurrences (all)	3	0	2
Myalgia			
subjects affected / exposed	1 / 41 (2.44%)	3 / 59 (5.08%)	4 / 33 (12.12%)
occurrences (all)	2	3	7
Back pain			
subjects affected / exposed	1 / 41 (2.44%)	1 / 59 (1.69%)	2 / 33 (6.06%)
occurrences (all)	1	1	2
Arthralgia			
subjects affected / exposed	6 / 41 (14.63%)	2 / 59 (3.39%)	4 / 33 (12.12%)
occurrences (all)	8	12	5
Arthritis			

subjects affected / exposed	0 / 41 (0.00%)	3 / 59 (5.08%)	3 / 33 (9.09%)
occurrences (all)	0	5	4
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 41 (4.88%)	0 / 59 (0.00%)	2 / 33 (6.06%)
occurrences (all)	2	0	2
COVID-19			
subjects affected / exposed	2 / 41 (4.88%)	6 / 59 (10.17%)	5 / 33 (15.15%)
occurrences (all)	2	6	5
Gastroenteritis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 59 (1.69%)	2 / 33 (6.06%)
occurrences (all)	0	1	2
Influenza			
subjects affected / exposed	0 / 41 (0.00%)	3 / 59 (5.08%)	1 / 33 (3.03%)
occurrences (all)	0	3	1
Nasopharyngitis			
subjects affected / exposed	0 / 41 (0.00%)	3 / 59 (5.08%)	2 / 33 (6.06%)
occurrences (all)	0	3	7
Oral candidiasis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 59 (0.00%)	2 / 33 (6.06%)
occurrences (all)	2	0	2
Pharyngitis			
subjects affected / exposed	0 / 41 (0.00%)	0 / 59 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	0	4
Respiratory tract infection			
subjects affected / exposed	1 / 41 (2.44%)	0 / 59 (0.00%)	2 / 33 (6.06%)
occurrences (all)	1	0	2
Upper respiratory tract infection			
subjects affected / exposed	3 / 41 (7.32%)	4 / 59 (6.78%)	1 / 33 (3.03%)
occurrences (all)	4	7	1
Upper respiratory tract infection bacterial			
subjects affected / exposed	0 / 41 (0.00%)	0 / 59 (0.00%)	3 / 33 (9.09%)
occurrences (all)	0	0	3
Urinary tract infection			

subjects affected / exposed	3 / 41 (7.32%)	5 / 59 (8.47%)	5 / 33 (15.15%)
occurrences (all)	5	6	5
Urinary tract infection bacterial			
subjects affected / exposed	0 / 41 (0.00%)	0 / 59 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	0	2
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 41 (0.00%)	0 / 59 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	0	2

Non-serious adverse events	Efavaleukin Alfa Low Dose		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 35 (77.14%)		
Nervous system disorders			
Tension headache			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	4		
Headache			
subjects affected / exposed	4 / 35 (11.43%)		
occurrences (all)	4		
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	5		
General disorders and administration site conditions			
Administration site inflammation			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	8		
Chest discomfort			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Injection site discolouration			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Pain			

subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Injection site inflammation			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Injection site oedema			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Injection site pain			
subjects affected / exposed	4 / 35 (11.43%)		
occurrences (all)	7		
Injection site pruritus			
subjects affected / exposed	7 / 35 (20.00%)		
occurrences (all)	39		
Injection site rash			
subjects affected / exposed	4 / 35 (11.43%)		
occurrences (all)	18		
Injection site reaction			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	4		
Injection site swelling			
subjects affected / exposed	6 / 35 (17.14%)		
occurrences (all)	23		
Injection site urticaria			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Injection site warmth			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Injection site erythema			
subjects affected / exposed	16 / 35 (45.71%)		
occurrences (all)	108		
Pyrexia			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Gastrointestinal disorders			

Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		
Constipation subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		
Vomiting subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		
Nausea subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1		
Gastritis subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 2		
Diarrhoea subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1		
Skin and subcutaneous tissue disorders			
Rash subjects affected / exposed occurrences (all)	3 / 35 (8.57%) 4		
Urticaria subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 2		
Musculoskeletal and connective tissue disorders			
Pain in extremity subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		
Myalgia subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1		
Back pain subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		
Arthralgia			

subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Arthritis			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
COVID-19			
subjects affected / exposed	4 / 35 (11.43%)		
occurrences (all)	4		
Gastroenteritis			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	3		
Oral candidiasis			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Respiratory tract infection			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	4 / 35 (11.43%)		
occurrences (all)	7		
Upper respiratory tract infection bacterial			

subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) Urinary tract infection bacterial subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0 1 / 35 (2.86%) 2 0 / 35 (0.00%) 0		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 August 2021	The following updates were made: • The efficacy analysis set was updated to include all participants randomized in the study and not those who have received at least 1 dose of investigation product. • Added the 2019 European League Against Rheumatism (EULAR)/ACR criteria, lupus narrative and prior history of BILAG domains to the Schedule of Activities (SoA). • Updated BILAG reference and scoring. • Added exploratory endpoint. • Removed PGIC baseline assessment from SoA. • Added blinded samples to protocol. • Added study adjudication language. • Updated the first data monitoring committee (DMC) meeting for safety to occur after the first 20 participants completed the Week 12 visit. • Added a subsection (Risk Assessment) to include guidance to sites regarding coronavirus disease 2019 (COVID-19). • Updated eligibility criteria. • Changed numbering of rescreening attempts from 2 to 3. • Included guidance on which adverse events lead to withholding or permanently discontinuing efavaleukin alfa. • Updated vital signs section. • Provided clarification for "decision by sponsor" as a reason to remove participant from study. • Included guidance for the investigator to repeat any labs that are considered to be clinically significant to rule out laboratory error. • Removed the Phadia assay being used on anti-double stranded DNA (anti-dsDNA) to determine eligibility. • Included required alignments with current Amgen protocol template. • Administrative and editorial changes.

01 September 2022	The following updates were made: • Removed requirement for a separate blinded joint assessor. • Clarified that the same assessor must perform efficacy assessments at every time point for a given participant. • Improved clarity of the definition of SRI-4 response and BICLA response. • Clarified that for arthritis to be scored, affected joints must have involved small joints in hands, wrists or a combination of joints in hands and wrists. • Endpoints were updated. • SoA was updated. • Clarified blood collection timepoints. • Updated statistical hypothesis. • Human Exposure and Risk Assessment were updated. • Clarified that prior to randomization, the investigator must have confirmed disease activity and compliance and stability of SLE treatment. • Updated justification for Investigational Product Dose. • Updated eligibility assessment order. • Updated end of study definition. • Clarified safety follow-up. • Provided instructions for scheduling early termination visit. • Updated interim analysis language. • Added biomarker discovery section. • Updated inclusion and exclusion criteria. • Updated information collected for screen failure. • Updated list of excluded medications/treatment. • Included a footnote in Analyte Listing table. • Described that individuals who did not meet criteria for participation could be rescreened up to 3 times. • Clarified lab retests required during screening should be approved by the sponsor. • Removed instruction that participants who screen failed should wait before being rescreened. • Provided specific instructions for capturing in injection site reaction as an adverse event. • Antibody Testing Procedures were updated. • Updated language for safety collection and reporting of serious adverse events. • Removed organ involvement as a baseline covariate on treatment effect. • Incorporated abbreviated study name. • Administrative and editorial changes.
21 October 2022	The following updates were made: • Added back the requirement for an independent blinded joint evaluator to conduct joint count assessments (number of tender and swollen joints). • Incorporated administrative and editorial changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

This study was discontinued early due to meeting predefined futility criteria at its third interim analysis.

Notes: