Clinical trial results:
A Multicentre, Randomised, Double-blind, Placebo-controlled, Phase 3 Study Evaluating the Efficacy and Safety of Two Doses of Anifrolumab in Adult Subjects with Active Systemic Lupus Erythematosus

Summary

EudraCT number	2014-004633-96
Trial protocol	GB DE HU PL RO IT
Global end of trial date	23 August 2018

Results information

Result version number	v1 (current)
This version publication date	18 December 2019
First version publication date	18 December 2019

Trial information

Trial identification

Sponsor protocol code	D3461C00005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02446912
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca AB
Sponsor organisation address	Forskargatan 18, Sudertalje, Sweden, 151 85
Public contact	Global Clinical Leader, AstraZeneca AB, +46 317761000, ClinicalTrialTransparency@astrazeneca.com
Scientific contact	Global Clinical Leader, AstraZeneca AB, +46 317761000, ClinicalTrialTransparency@astrazeneca.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	23 August 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 August 2018
Global end of trial reached?	Yes
Global end of trial date	23 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial was to evaluate the effect of anifrolumab 300 mg compared to placebo on disease activity as measured by the difference in the proportion of participants who achieve an systemic lupus erythematosus (SLE) responder index of ≥4 (SRI[4]) at Week 52.

Protection of trial subjects:

The study was performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and are consistent with ICH/GCP, applicable regulatory requirements and the AstraZeneca policy on Bioethics and Human Biological Samples.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 June 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	New Zealand: 1
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Korea, Republic of: 9
Country: Number of subjects enrolled	Taiwan: 9
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Hungary: 18
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Poland: 69
Country: Number of subjects enrolled	Romania: 27
Country: Number of subjects enrolled	Ukraine: 36
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	Argentina: 6
Country: Number of subjects enrolled	Brazil: 14
Country: Number of subjects enrolled	Chile: 7
Country: Number of subjects enrolled	Colombia: 10
Country: Number of subjects enrolled	Peru: 25
Country: Number of subjects enrolled	United States: 186

Country: Number of subjects enrolled	Israel: 12
Worldwide total number of subjects	457
EEA total number of subjects	137

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)	437
From 65 to 84 years	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the trial at 123 sites in 18 countries worldwide.

Pre-assignment

Screening details:

Participants reported to the medical screening facility/clinical study site for the eligibility screening within 30 days of first study drug administration. Out of the 847 participants screened for the trial, 390 participants were screen failures and were not randomized and 457 participants were randomized onto the trial.

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, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Anifrolumab 150 mg

Arm description:

Anifrolumab (150 mg) administered via an intravenous infusion (IV) every 4 weeks for up to 48 weeks (13 doses)

Arm type	Experimental
Investigational medicinal product name	Anifrolumab
Investigational medicinal product code	MEDI-546
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

150 mg anifrolumab administered via a controlled intravenous infusion (IV) pump into a peripheral vein over at least 30 minutes, every 4 weeks.

Arm title	Anifrolumab 300 mg

Arm description:

Anifrolumab (300 mg) administered via an intravenous infusion (IV) every 4 weeks for up to 48 weeks (13 doses)

Arm type	Experimental
Investigational medicinal product name	Anifrolumab
Investigational medicinal product code	MEDI-546
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

300 mg anifrolumab administered via a controlled intravenous infusion (IV) pump into a peripheral vein over at least 30 minutes, every 4 weeks.

Arm title	Placebo

Arm description:

Matching placebo administered via an intravenous infusion (IV) every 4 weeks for up to 48 weeks (13 doses)

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Matching placebo administered via a controlled intravenous infusion (IV) pump into a peripheral vein over at least 30 minutes, every 4 weeks.

Number of subjects in period 1	Anifrolumab 150 mg	Anifrolumab 300 mg	Placebo
Started	93	180	184
Participants who completed week 52	80	153	157
Completed	75	145	149
Not completed	18	35	35
Severe non-compliance to protocol	1	-	1
Consent withdrawn by subject	10	15	15
Adverse event, non-fatal	3	13	5
Condition under investigation worsened	-	1	1
Miscellaneous	2	2	4
Study-specific withdrawal criteria	1	-	-
Lost to follow-up	-	-	2
Lack of efficacy	1	4	7

Baseline characteristics

Reporting groups	
Reporting group title	Anifrolumab 150 mg
Reporting group description:	
Anifrolumab (150 mg) administered via an intravenous infusion (IV) every 4 weeks for up to 48 weeks (13 doses)	
Reporting group title	Anifrolumab 300 mg
Reporting group description:	
Anifrolumab (300 mg) administered via an intravenous infusion (IV) every 4 weeks for up to 48 weeks (13 doses)	
Reporting group title	Placebo
Reporting group description:	
Matching placebo administered via an intravenous infusion (IV) every 4 weeks for up to 48 weeks (13 doses)	

Reporting group values	Anifrolumab 150 mg	Anifrolumab 300 mg	Placebo
Number of subjects	93	180	184
Age Categorical Units: Subjects			
<18 years	0	0	0
≥18 to <65 years	90	169	178
≥65 years	3	11	6
Age Continuous Units: Years			
arithmetic mean	40.8	42.0	41.0
standard deviation	± 12.05	± 11.99	± 12.30
Sex: Female, Male Units: Subjects			
Female	86	165	171
Male	7	15	13
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	1
Asian	8	11	5
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	14	29	23
White	64	125	137
More than one race	0	0	0
Unknown or Not Reported	7	15	18
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	20	32	35
Not Hispanic or Latino	73	148	149
Unknown or Not Reported	0	0	0
Height Units: cm			
arithmetic mean	164.02	162.99	163.10
standard deviation	± 8.208	± 7.829	± 8.030

Weight			
Units: kg			
arithmetic mean	73.57	75.36	74.69
standard deviation	± 19.469	± 20.343	± 19.332
Body Mass Index (BMI)			
Units: kg/m^2			
arithmetic mean	27.31	28.25	28.09
standard deviation	± 6.812	± 6.899	± 7.145

Reporting group values	Total		
Number of subjects	457		
Age Categorical			
Units: Subjects			
<18 years	0		
≥18 to <65 years	437		
≥65 years	20		
Age Continuous			
Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: Subjects			
Female	422		
Male	35		
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	1		
Asian	24		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	66		
White	326		
More than one race	0		
Unknown or Not Reported	40		
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	87		
Not Hispanic or Latino	370		
Unknown or Not Reported	0		
Height			
Units: cm			
arithmetic mean			
standard deviation	-		
Weight			
Units: kg			
arithmetic mean			
standard deviation	-		
Body Mass Index (BMI)			
Units: kg/m^2			
arithmetic mean			
standard deviation	-		

End points reporting groups

Reporting group title	Anifrolumab 150 mg
Reporting group description:	
Anifrolumab (150 mg) administered via an intravenous infusion (IV) every 4 weeks for up to 48 weeks (13 doses)	
Reporting group title	Anifrolumab 300 mg
Reporting group description:	
Anifrolumab (300 mg) administered via an intravenous infusion (IV) every 4 weeks for up to 48 weeks (13 doses)	
Reporting group title	Placebo
Reporting group description:	
Matching placebo administered via an intravenous infusion (IV) every 4 weeks for up to 48 weeks (13 doses)	
Subject analysis set title	Anifrolumab 150 mg high IFN test results subgroup
Subject analysis set type	Full analysis
Subject analysis set description:	
Anifrolumab (150 mg) administered via an intravenous infusion (IV) every 4 weeks for up to 48 weeks (13 doses). Participants with high IFN test results.	
Subject analysis set title	Anifrolumab 150 mg low IFN test results subgroup
Subject analysis set type	Full analysis
Subject analysis set description:	
Anifrolumab (150 mg) administered via an intravenous infusion (IV) every 4 weeks for up to 48 weeks (13 doses). Participants with low IFN test results.	
Subject analysis set title	Anifrolumab 300 mg high IFN test results subgroup
Subject analysis set type	Full analysis
Subject analysis set description:	
Anifrolumab (300 mg) administered via an intravenous infusion (IV) every 4 weeks for up to 48 weeks (13 doses). Participants with high IFN test results.	
Subject analysis set title	Anifrolumab 300 mg low IFN test results subgroup
Subject analysis set type	Full analysis
Subject analysis set description:	
Anifrolumab (300 mg) administered via an intravenous infusion (IV) every 4 weeks for up to 48 weeks (13 doses). Participants with low IFN test results.	
Subject analysis set title	Placebo high IFN test results subgroup
Subject analysis set type	Full analysis
Subject analysis set description:	
Matching placebo administered via an intravenous infusion (IV) every 4 weeks for up to 48 weeks (13 cycles). Participants with high IFN test results.	
Subject analysis set title	Placebo low IFN test results subgroup
Subject analysis set type	Full analysis
Subject analysis set description:	
Matching placebo administered via an intravenous infusion (IV) every 4 weeks for up to 48 weeks (13 cycles). Participants with low IFN test results.	
Subject analysis set title	Anifrolumab 150 mg Baseline OCS ≥10 mg/day
Subject analysis set type	Full analysis
Subject analysis set description:	
Anifrolumab (150 mg) administered via an intravenous infusion (IV) every 4 weeks for up to 48 weeks (13 doses). Participants with a baseline oral corticosteroid (OCS) dose of ≥10 mg/day.	
Subject analysis set title	Anifrolumab 300 mg Baseline OCS ≥10 mg/day
Subject analysis set type	Full analysis
Subject analysis set description:	
Anifrolumab (300 mg) administered via an intravenous infusion (IV) every 4 weeks for up to 48 weeks	

(13 doses). Participants with a baseline oral corticosteroid (OCS) dose of ≥10 mg/day.

Subject analysis set title	Placebo Baseline OCS ≥10 mg/day
Subject analysis set type	Full analysis

Subject analysis set description:

Matching placebo administered via an intravenous infusion (IV) every 4 weeks for up to 48 weeks (13 cycles). Participants with a baseline oral corticosteroid (OCS) dose of ≥10 mg/day.

Subject analysis set title	Anifrolumab 150 mg CLASI Activity Score ≥10
Subject analysis set type	Full analysis

Subject analysis set description:

Anifrolumab (150 mg) administered via an intravenous infusion (IV) every 4 weeks for up to 48 weeks (13 doses). Participants with Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) activity score of ≥10.

Subject analysis set title	Anifrolumab 300 mg CLASI Activity Score ≥10
Subject analysis set type	Full analysis

Subject analysis set description:

Anifrolumab (300 mg) administered via an intravenous infusion (IV) every 4 weeks for up to 48 weeks (13 doses). Participants with Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) activity score of ≥10.

Subject analysis set title	Placebo CLASI Activity Score ≥10
Subject analysis set type	Full analysis

Subject analysis set description:

Matching placebo administered via an intravenous infusion (IV) every 4 weeks for up to 48 weeks (13 cycles). Participants with a Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) Activity Score ≥10.

Primary: Number of Participants Who Achieved a Systemic Lupus Erythematosus (SLE) Responder Index ≥4 (SRI[4]) at Week 52 (Original Analysis with Restricted Medication Rules)

End point title	Number of Participants Who Achieved a Systemic Lupus Erythematosus (SLE) Responder Index ≥4 (SRI[4]) at Week 52 (Original Analysis with Restricted Medication Rules)

End point description:

SRI(4) was defined as meeting all of the following criteria:

Reduction from baseline of ≥4 points in the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K)
No new organ systems affected, defined by 1 or more British Isles Lupus Assessment Group (BILAG-2004) A or 2 or more BILAG-2004 B items
No worsening from baseline in participants lupus disease activity. Worsening was defined as an increase of ≥0.30 points on a 3-point Physician's Global Assessment (PGA) visual analogue scale (VAS)
No discontinuation of investigational product and no use of restricted medications beyond the pre-specified analysis threshold.

End point type	Primary

End point timeframe:

Week 52

End point values	Anifrolumab 150 mg	Anifrolumab 300 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	93	180	184	
Units: Participants	35	65	74	

Statistical analyses

Statistical analysis title	Analysis of Treatment Difference
Comparison groups	Anifrolumab 300 mg v Placebo
Number of subjects included in analysis	364
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.412 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportions
Point estimate	-4.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.2
upper limit	5.8

Notes:

[1] - Nominal p-value

Statistical analysis title	Analysis of Treatment Difference

Statistical analysis description:

The difference in estimates and associated 95% CI are weighted and are calculated using a stratified Cochran-Mantel-Haenszel (CMH) approach, with stratification factors (SLEDAI-2K score at screening [<10 points vs >= 10 points], Week 0 OCS dose [<10 mg/day vs >=10 mg/day prednisone or equivalent] and type I IFN gene signature test result at screening [high vs low]).

Comparison groups	Anifrolumab 150 mg v Placebo
Number of subjects included in analysis	277
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in proportions
Point estimate	-2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.7
upper limit	9.6

Secondary: Number of Participants Who Achieved a Systemic lupus erythematosus (SLE) Responder Index of ≥4 at Week 52 in the Interferon (IFN) Test-High Sub-Group (Original Analysis with Restricted Medication Rules)

End point title	Number of Participants Who Achieved a Systemic lupus erythematosus (SLE) Responder Index of ≥4 at Week 52 in the Interferon (IFN) Test-High Sub-Group (Original Analysis with Restricted Medication Rules)

End point description:

SRI(4) was defined as meeting all of the following criteria:

Reduction from baseline of ≥4 points in the SLEDAI-2K
No new organ systems affected, defined by 1 or more BILAG-2004) A or 2 or more BILAG-2004 B
No worsening from baseline in participants lupus disease activity. Worsening was defined as an increase of ≥0.30 points on a 3-point PGA VAS
No discontinuation of investigational product and no use of restricted medications beyond the pre-specified analysis threshold.

End point type	Secondary

End point timeframe:

Week 52

End point values	Anifrolumab 150 mg high IFN test results subgroup	Anifrolumab 300 mg high IFN test results subgroup	Placebo high IFN test results subgroup	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	76	148	151	
Units: Participants	30	53	59	

Statistical analyses

Statistical analysis title	Analysis of Treatment Difference
Comparison groups	Anifrolumab 300 mg high IFN test results subgroup v Placebo high IFN test results subgroup
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.549 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportions
Point estimate	-3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.4
upper limit	7.6

Notes:

[2] - Nominal p-value

Secondary: Number of Participants Who Achieved and Maintained an Oral Corticosteroid (OCS) Dose of ≤7.5 mg/day in the Sub-group of Participants with Baseline OCS ≥10 mg/day (Original Analysis with Restricted Medication Rules)

End point title	Number of Participants Who Achieved and Maintained an Oral Corticosteroid (OCS) Dose of ≤7.5 mg/day in the Sub-group of Participants with Baseline OCS ≥10 mg/day (Original Analysis with Restricted Medication Rules)

End point description:

Maintained OCS reduction was defined by meeting all the following criteria:

Achieve an OCS dose of ≤7.5 mg/day prednisone or equivalent by Week 40
Maintain an OCS dose ≤7.5 mg/day prednisone or equivalent from Week 40 to Week 52
No discontinuation of investigational product and no use of restricted medications beyond the pre-specified analysis threshold.

End point type	Secondary

End point timeframe:

Week 52

End point values	Anifrolumab 150 mg Baseline OCS ≥10 mg/day	Anifrolumab 300 mg Baseline OCS ≥10 mg/day	Placebo Baseline OCS ≥10 mg/day	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	48	103	102	
Units: Participants	17	42	33	

Statistical analyses

Statistical analysis title	Analysis of Treatment Difference
Comparison groups	Anifrolumab 300 mg Baseline OCS ≥10 mg/day v Placebo Baseline OCS ≥10 mg/day
Number of subjects included in analysis	205
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.18 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportions
Point estimate	8.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.1
upper limit	21.9

Notes:

[3] - Nominal p-value

Secondary: Number of Participants with a ≥50% reduction in CLASI Activity Score at Week 12 in the sub-group of Participants with Baseline CLASI Activity Score ≥10 (Original Analysis with Restricted Medication Rules)

End point title	Number of Participants with a ≥50% reduction in CLASI Activity Score at Week 12 in the sub-group of Participants with Baseline CLASI Activity Score ≥10 (Original Analysis with Restricted Medication Rules)

End point description:

50% reduction in Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) activity score compared to baseline was defined by meeting all of the following criteria:

Achieve ≥50% reduction of CLASI activity score at Week 12 compared to baseline
No discontinuation of investigational product and no use of restricted medications beyond the pre-specified analysis threshold before assessment.

End point type	Secondary

End point timeframe:

Week 12

End point values	Anifrolumab 150 mg CLASI Activity Score ≥10	Anifrolumab 300 mg CLASI Activity Score ≥10	Placebo CLASI Activity Score ≥10	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	30	58	54	
Units: Participants	15	24	14	

Statistical analyses

Statistical analysis title	Analysis of Treatment
Comparison groups	Anifrolumab 300 mg CLASI Activity Score ≥10 v Placebo CLASI Activity Score ≥10
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.054 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportions
Point estimate	17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	34.3

Notes:

[4] - Nominal p-value

Secondary: Number of Participants Who Achieved a Systemic Lupus Erythematosus (SLE) Responder Index of ≥4 (SRI[4]) at Week 24 (Original Analysis with Restricted Medication Rules)

End point title	Number of Participants Who Achieved a Systemic Lupus Erythematosus (SLE) Responder Index of ≥4 (SRI[4]) at Week 24 (Original Analysis with Restricted Medication Rules)

End point description:

SRI(4) was defined as meeting all of the following criteria:

Reduction from baseline of ≥4 points in the SLEDAI-2K
No new organ systems affected as defined by 1 or more BILAG-2004 A or 2 or more BILAG-2004 B items
No worsening from baseline in participants lupus disease activity. Worsening was defined as an increase of ≥0.30 points on a 3-point PGA VAS
No discontinuation of investigational product and no use of restricted medications beyond the pre-specified threshold.

End point type	Secondary

End point timeframe:

Week 24

End point values	Anifrolumab 150 mg	Anifrolumab 300 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	93	180	184	
Units: Participants	34	74	75	

Statistical analyses

Statistical analysis title	Analysis of Treatment Difference
Comparison groups	Anifrolumab 300 mg v Placebo
Number of subjects included in analysis	364
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.905 [5]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportions
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.4
upper limit	10.6

Notes:

[5] - Nominal p-value

Secondary: Annualized Flare Rate

End point title	Annualized Flare Rate

End point description:

A flare was defined as either 1 or more new British Isle Lupus Assessment Group (BILAG-2004) A or 2 or more new BILAG-2004 B items compared to the previous visit. The occurrence of a new flare was checked for each available visit versus the previous available visit up to Week 52. If no new flares occurred, the number of flares was set to 0. Otherwise all flares were counted leading to the maximum number of flares of 13. The annualized flare rate was calculated as the number of flares divided by the flare exposure time in days multiplied with 365.25 (1 year). The flare exposure time is the time up to Week 52 (date of BILAG-2004 assessment at Week 52) or up to the date of last available BILAG-2004 assessment.

End point type	Secondary

End point timeframe:

Baseline to Week 52

End point values	Anifrolumab 150 mg	Anifrolumab 300 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	93	180	184	
Units: Annualized flare rate ratio				
number (not applicable)	0.62	0.60	0.72	

Statistical analyses

Statistical analysis title	Analysis of Treatment Difference

Statistical analysis description:

Analysed using a negative binomial regression model. The response variable in the model is the number of flares over the 52-week treatment period. The model includes covariates of treatment group, and the stratification factors (SLEDAI-2K score at screening [<10 points vs >=10 points], Week 0 OCS dose [<10 mg/day vs >=10 mg/day prednisone or equivalent] and type I IFN gene signature test result at screening [high vs low]). The logarithm of the follow-up time is used as an offset variable

Comparison groups	Anifrolumab 300 mg v Placebo
Number of subjects included in analysis	364
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.258 [6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Rate Ratio
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.14

Notes:

[6] - Nominal p-value

Secondary: Number of Participants who Met the Criteria for British Isles Lupus Assessment Group-based Composite Lupus Assessment (BICLA) Response (Original Analysis with Restricted Medication Rules)

End point title	Number of Participants who Met the Criteria for British Isles Lupus Assessment Group-based Composite Lupus Assessment (BICLA) Response (Original Analysis with Restricted Medication Rules)

End point description:

A BICLA responder was achieved if all of the following criteria was met:

All criteria related to SRI(4) (please see primary endpoint) plus:
Reduction of all baseline BILAG-2004 A to B/C/D and baseline BILAG-2004 B to C/D, and no BILAG-2004 worsening in other organ systems, as defined by 1 or more BILAG-2004 A or 1 or more new BILAG-2004 B item
No discontinuation of investigational product and no use of restricted medications beyond the revised post-hoc analysis threshold before assessment.

End point type	Secondary

End point timeframe:

Week 52

End point values	Anifrolumab 150 mg	Anifrolumab 300 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	93	180	184	
Units: Participants	27	67	49	

Statistical analyses

Statistical analysis title	Analysis of Treatment Difference

Statistical analysis description:

The difference in estimates and associated 95% CI are weighted and are calculated using a stratified Cochran-Mantel-Haenszel (CMH) approach, with stratification factors (SLEDAI-2K score at screening [<10 points vs >= 10 points], Week 0 OCS dose [<10 mg/day vs >=10 mg/day prednisone or equivalent] and type I IFN gene signature test result at screening [high vs low]).

Comparison groups	Anifrolumab 300 mg v Placebo
Number of subjects included in analysis	364
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in proportions
Point estimate	10.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	19.7

Secondary: Number of Participants Reporting One or More Adverse Events (AEs)

End point title	Number of Participants Reporting One or More Adverse Events (AEs)

End point description:

An AE is defined as any untoward medical occurrence in a clinical investigation participant administered a drug; it does not necessarily have to have a causal relationship with this treatment. AEs were collected throughout the duration of the study, from baseline until end of follow-up (a maximum of 12 weeks post last dose [Week 48]), or until Week 52 for participants who enrolled onto the long term extension (LTE). The reported value is inclusive of serious and non-serious AEs.

End point type	Secondary

End point timeframe:

Baseline to End of Trial (Maximum of 60 weeks)

End point values	Anifrolumab 150 mg	Anifrolumab 300 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	93	180	184	
Units: Participants	80	161	145	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Reporting One or More Adverse Events of Special Interest (AESI)

End point title	Number of Participants Reporting One or More Adverse Events of Special Interest (AESI)

End point description:

An AESI is an AE of scientific and medical concern specific to understanding biologics and requires close monitoring and rapid communication by the Investigator to the Sponsor/Sponsor's delegate. An AESI may be serious or nonserious. The events of interest are serious infections, including non opportunistic serious infections, opportunistic infections, anaphylaxis, malignancy, herpes zoster, TB (including latent TB), influenza, vasculitis (non-SLE), and MACE (including stroke, MI, or cardiovascular death). AEs were collected throughout the duration of the study, from baseline until end of follow-up (a maximum of 12 weeks post last dose [Week 48]), or until Week 52 for participants who enrolled onto the long term extension (LTE).

End point type	Secondary

End point timeframe:

Baseline to End of Trial (Maximum of 60 weeks)

End point values	Anifrolumab 150 mg	Anifrolumab 300 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	93	180	184	
Units: Participants	11	23	18	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Markedly Abnormal Vital Signs

End point title	Number of Participants with Markedly Abnormal Vital Signs

End point description:

Vital signs included oral temperature, blood pressure (BP), pulse rate, and respiratory rate.
Vital signs were collected throughout the duration of the study, from baseline until end of follow-up (a maximum of 12 weeks post last dose [Week 48]), or until Week 52 for participants who enrolled onto the long term extension (LTE).

End point type	Secondary

End point timeframe:

Baseline to End of Trial (Maximum of 60 weeks)

End point values	Anifrolumab 150 mg	Anifrolumab 300 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	93	180	184	
Units: Participants	14	36	46	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Markedly Abnormal Physical Examinations

End point title	Number of Participants with Markedly Abnormal Physical Examinations

End point description:

Physical examinations included height and weight. Participants were weighed at each study visit and any medically significant changes were reported.
Physical examination values were collected throughout the duration of the study, from baseline until end of follow-up (a maximum of 12 weeks post last dose [Week 48]), or until Week 52 for participants who enrolled onto the long term extension (LTE).

End point type	Secondary

End point timeframe:

Baseline to End of Trial (Maximum of 60 weeks)

End point values	Anifrolumab 150 mg	Anifrolumab 300 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	93	180	184	
Units: Participants	2	2	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Markedly Abnormal ECG Scores

End point title	Number of Participants with Markedly Abnormal ECG Scores

End point description:

ECGs documented the date, time, heart rate, QRS duration, PR interval, RR interval, QT, and corrected QT interval, which were calculated using the Fridericia formula. The investigator judged the overall interpretation as normal or abnormal, and if abnormal it was decided as to whether or not the abnormality was clinically significant or not clinically significant.

End point type	Secondary

End point timeframe:

Baseline to End of Trial (Maximum of 60 weeks)

End point values	Anifrolumab 150 mg	Anifrolumab 300 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	93	180	184	
Units: Participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Mild To Moderate Lupus Flare Evaluated by Modified SELENA-SLEDAI Flare Index

End point title	Number of Participants With Mild To Moderate Lupus Flare Evaluated by Modified SELENA-SLEDAI Flare Index

End point description:

The modified SELENA flare index was completed by the Investigator or delegated/qualified physician. Assessment of flares were scored in comparison to the participant's previous visit and should only include findings which, in the opinion of the Investigator, are due to systemic lupus erythematosus (SLE) disease activity within that timeframe. Flare was defined as any 1 criterion present in either the Mild/Moderate Flare or Severe Flare categories.

Number of flares were collected throughout the duration of the study, from baseline until end of follow-up (a maximum of 12 weeks post last dose [Week 48]), or until Week 52 for participants who enrolled onto the long term extension (LTE).

End point type	Secondary

End point timeframe:

Baseline to End of Trial (Maximum of 60 weeks)

End point values	Anifrolumab 150 mg	Anifrolumab 300 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	93	180	184	
Units: Participants	38	58	67	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Markedly Abnormal Laboratory Tests

End point title	Number of Participants with Markedly Abnormal Laboratory Tests

End point description:

Laboratory tests were collected at central clinical laboratories and included hematology, serum chemistry and urinalysis tests. Laboratory values were collected throughout the duration of the study,

from baseline until end of follow-up (a maximum of 12 weeks post last dose [Week 48]), or until Week 52 for participants who enrolled onto the long term extension (LTE).

End point type	Secondary

End point timeframe:

Baseline to End of Trial (Maximum of 60 weeks)

End point values	Anifrolumab 150 mg	Anifrolumab 300 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	93	180	184	
Units: Participants	44	71	87	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Suicidal Ideation or Behaviour Assessed via the Columbia Suicide Severity Rating Scale (C-SSRS)

End point title	Number of Participants with Suicidal Ideation or Behaviour Assessed via the Columbia Suicide Severity Rating Scale (C-SSRS)

End point description:

The C-SSRS is an assessment tool that evaluates suicidal ideation and behavior. Number of participants with suicidal ideation or behavior was defined as the number of participants who answered "yes" at any time during the treatment period (Baseline to Week 52) to one of the 10 categories:
Category 1: Wish to be dead
Category 2: Non-specific active suicidal thoughts
Category 3: Active suicidal ideation with any methods (not plan) without intent to act
Category 4: Active suicidal ideation with some intent to act, without specific plan
Category 5: Active suicidal ideation with specific plan and intent
Category 6: Preparatory acts or behavior
Category 7: Aborted attempt
Category 8: Interrupted attempt
Category 9: Actual attempt (non-fatal)
Category 10: Completed suicide

End point type	Secondary

End point timeframe:

Baseline to Week 52

End point values	Anifrolumab 150 mg	Anifrolumab 300 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	93	180	184	
Units: Participants				
Suicidal ideation|	1	2	2	
Suicidal behaviour|	0	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Personal Health Questionnaire Depression Scale-8 (PHQ-8) Score

End point title	Change from Baseline in Personal Health Questionnaire Depression Scale-8 (PHQ-8) Score

End point description:

PHQ-8 is a 8-item self-report scale, all items are rated on a score of 0-3, for a total range of 0-24. PHQ-8 assesses symptoms of depression over the previous 2 weeks. Higher scores indicate more depressive symptoms. A negative change from baseline score indicates improvement in symptoms.

End point type	Secondary

End point timeframe:

Baseline to Week 52

End point values	Anifrolumab 150 mg	Anifrolumab 300 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71	130	138	
Units: Score on a Scale				
arithmetic mean (standard deviation)	-2.1 (± 4.43)	-2.7 (± 5.58)	-1.7 (± 5.40)	

Statistical analyses

No statistical analyses for this end point

Post-hoc: Number of Participants Who Achieved a Systemic Lupus Erythematosus (SLE) Responder Index ≥4 (SRI[4]) at Week 52 (Post-Hoc Analysis with Revised Restricted Medication Rules)

End point title	Number of Participants Who Achieved a Systemic Lupus Erythematosus (SLE) Responder Index ≥4 (SRI[4]) at Week 52 (Post-Hoc Analysis with Revised Restricted Medication Rules)

End point description:

SRI(4) was defined as meeting all of the following criteria:

Reduction from baseline of ≥4 points in the SLEDAI-2K
No new organ systems affected, defined by 1 or more BILAG-2004 A or 2 or more BILAG-2004 B items
No worsening from baseline in lupus disease activity. Worsening defined as an increase of ≥0.30 points on a 3-point PGA VAS
No discontinuation of investigational product and no use of restricted medications beyond the revised post-hoc allowed threshold.

Revised rules were designed to be more clinically appropriate, capture intent of protocol, minimize the

risk of restricted medications confounding efficacy, and to allow appropriate quantification and interpretation of the relevant endpoints.

End point type	Post-hoc

End point timeframe:

Week 52

End point values	Anifrolumab 150 mg	Anifrolumab 300 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	93	180	184	
Units: Participants	45	84	79	

Statistical analyses

Statistical analysis title	Analysis of Treatment Difference

Statistical analysis description:

The difference in estimates and associated 95% CI are weighted and are calculated using a stratified Cochran-Mantel-Haenszel (CMH) approach, with stratification factors (SLEDAI-2K score at screening [<10 points vs >= 10 points], Week 0 OCS dose [<10 mg/day vs >=10 mg/day prednisone or equivalent] and type I IFN gene signature test result at screening [high vs low]).

Comparison groups	Anifrolumab 300 mg v Placebo
Number of subjects included in analysis	364
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4555 [7]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportions
Point estimate	3.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.3
upper limit	14.1

Notes:

[7] - Nominal p-value

Statistical analysis title	Analysis of Treatment Difference
Comparison groups	Anifrolumab 150 mg v Placebo
Number of subjects included in analysis	277
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in proportions
Point estimate	5.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.7
upper limit	17.8

Post-hoc: Number of Participants Who Achieved a Systemic Lupus Erythematosus (SLE) Responder Index of ≥4 at Week 52 in the Interferon (IFN) Test-High Sub-Group (Post-Hoc Analysis with Revised Restricted Medication Rules)

End point title	Number of Participants Who Achieved a Systemic Lupus Erythematosus (SLE) Responder Index of ≥4 at Week 52 in the Interferon (IFN) Test-High Sub-Group (Post-Hoc Analysis with Revised Restricted Medication Rules)

End point description:

SRI(4) was defined as meeting all of the following criteria:

Reduction from baseline of ≥4 points in the SLEDAI-2K
No new organ systems affected, defined by 1 or more BILAG-2004 A or 2 or more BILAG-2004 B items
No worsening from baseline in lupus disease activity. Worsening defined as an increase of ≥0.30 points on a 3-point PGA VAS
No discontinuation of investigational product and no use of restricted medications beyond the revised post-hoc analysis threshold.

Revised rules were designed to be more clinically appropriate, capture intent of protocol, minimize the risk of restricted medications confounding efficacy, and to allow appropriate quantification and interpretation of the relevant endpoints.

End point type	Post-hoc

End point timeframe:

Week 52

End point values	Anifrolumab 150 mg high IFN test results subgroup	Anifrolumab 300 mg high IFN test results subgroup	Placebo high IFN test results subgroup	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	76	148	151	
Units: Participants	40	71	63	

Statistical analyses

Statistical analysis title	Analysis of Treatment Difference
Comparison groups	Anifrolumab 300 mg high IFN test results subgroup v Placebo high IFN test results subgroup

Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	= 0.261 [9]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportions
Point estimate	6.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	17.7

Notes:

[8] - The difference in estimates and associated 95% CI are weighted and are calculated using a stratified Cochran-Mantel-Haenszel (CMH) approach, with stratification factors (SLEDAI-2K score at screening [<10 points vs >= 10 points], Week 0 OCS dose [<10 mg/day vs >=10 mg/day prednisone or equivalent] and type I IFN gene signature test result at screening [high vs low]).
[9] - Nominal p-value

Post-hoc: Number of Participants Who Achieved and Maintained an Oral Corticosteroid (OCS) Dose of ≤7.5 mg/day in the Sub-group of Participants with Baseline OCS ≥10 mg/day (Post-Hoc Analysis with Revised Restricted Medication Rules)

End point title	Number of Participants Who Achieved and Maintained an Oral Corticosteroid (OCS) Dose of ≤7.5 mg/day in the Sub-group of Participants with Baseline OCS ≥10 mg/day (Post-Hoc Analysis with Revised Restricted Medication Rules)

End point description:

Maintained OCS reduction was defined by meeting all of the following criteria:

Achieve an OCS dose of ≤7.5 mg/day prednisone or equivalent by Week 40
Maintain an OCS dose ≤7.5 mg/day prednisone or equivalent from Week 40 to Week 52
No discontinuation of investigational product and no use of restricted medications beyond the revised post-hoc analysis threshold.

Rules regarding use of NSAIDS (criteria used to define Revised rules were designed to be more clinically appropriate, capture intent of protocol, minimize the risk of restricted medication confounding efficacy, and to allow appropriate quantification and interpretation of the relevant endpoints.

End point type	Post-hoc

End point timeframe:

Week 52

End point values	Anifrolumab 150 mg Baseline OCS ≥10 mg/day	Anifrolumab 300 mg Baseline OCS ≥10 mg/day	Placebo Baseline OCS ≥10 mg/day	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	48	103	102	
Units: Participants	24	50	33	

Statistical analyses

Statistical analysis title	Analysis of Treatment Difference
Comparison groups	Anifrolumab 300 mg Baseline OCS ≥10 mg/day v Placebo Baseline OCS ≥10 mg/day
Number of subjects included in analysis	205
Analysis specification	Pre-specified
Analysis type	superiority[10]
P-value	= 0.013 [11]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportions
Point estimate	16.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.5
upper limit	29.8

Notes:

[10] - The difference in estimates and associated 95% CI are weighted and are calculated using a stratified Cochran-Mantel-Haenszel (CMH) approach, with stratification factors (SLEDAI-2K score at screening [<10 points vs >= 10 points], Week 0 OCS dose [<10 mg/day vs >=10 mg/day prednisone or equivalent] and type I IFN gene signature test result at screening [high vs low]).
[11] - Nominal p-value

Post-hoc: Number of Participants with a ≥50% reduction in CLASI Activity Score at Week 12 in the sub-group of Participants with Baseline CLASI Activity Score ≥10 (Post-Hoc Analysis with Revised Restricted Medication Rules)

End point title	Number of Participants with a ≥50% reduction in CLASI Activity Score at Week 12 in the sub-group of Participants with Baseline CLASI Activity Score ≥10 (Post-Hoc Analysis with Revised Restricted Medication Rules)

End point description:

50% reduction in Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) activity score compared to baseline was defined by meeting all the following criteria:

Achieve ≥50% reduction of CLASI activity score at Week 12 compared to baseline
No discontinuation of investigational product and no use of restricted medications beyond the revised post-hoc analysis threshold before assessment.

Revised rules were designed to be more clinically appropriate, capture intent of protocol, minimize the risk of restricted medication confounding efficacy, and to allow appropriate quantification and interpretation of the relevant endpoints..

End point type	Post-hoc

End point timeframe:

Week 12

End point values	Anifrolumab 150 mg CLASI Activity Score ≥10	Anifrolumab 300 mg CLASI Activity Score ≥10	Placebo CLASI Activity Score ≥10	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	30	58	54	
Units: Participants	16	25	14	

Statistical analyses

Statistical analysis title	Analysis of Treatment Differences
Comparison groups	Anifrolumab 300 mg CLASI Activity Score ≥10 v Placebo CLASI Activity Score ≥10
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority[12]
P-value	= 0.034 [13]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportions
Point estimate	18.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.4
upper limit	36

Notes:

[12] - The difference in estimates and associated 95% CI are weighted and are calculated using a stratified Cochran-Mantel-Haenszel (CMH) approach, with stratification factors (SLEDAI-2K score at screening [<10 points vs >= 10 points], Week 0 OCS dose [<10 mg/day vs >=10 mg/day prednisone or equivalent] and type I IFN gene signature test result at screening [high vs low]).
[13] - Nominal p-value

Post-hoc: Number of Participants Who Achieved a Systemic Lupus Erythematosus (SLE) Responder Index of ≥4 (SRI[4]) at Week 24 (Post-Hoc Analysis with Revised Restricted Medication Rules)

End point title	Number of Participants Who Achieved a Systemic Lupus Erythematosus (SLE) Responder Index of ≥4 (SRI[4]) at Week 24 (Post-Hoc Analysis with Revised Restricted Medication Rules)

End point description:

SRI(4) was defined as meeting all of the following criteria:

Reduction from baseline of ≥4 points in the SLEDAI-2K
No new organ systems affected, defined by 1 or more BILAG-2004 A or 2 or more BILAG-2004 B items
No worsening from baseline in lupus disease activity. Worsening defined as an increase of ≥0.30 points on a 3-point PGA VAS
No discontinuation of investigational product and no use of restricted medications beyond the revised post-hoc allowed threshold.

Rules regarding use of NSAIDS (criteria used to define participants as non-responders) were not implemented as intended per protocol and were not appropriate based on clinical practice (participant taking NSAIDs deemed as non-responder). Revised rules were designed to be more clinically appropriate, capture intent of protocol, minimize the risk of restricted medications confounding efficacy, and to allow appropriate quantification and interpretation of the relevant endpoints.

End point type	Post-hoc

End point timeframe:

Week 24

End point values	Anifrolumab 150 mg	Anifrolumab 300 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	93	180	184	
Units: Participants	40	83	79	

Statistical analyses

Statistical analysis title	Analysis of Treatment Difference
Comparison groups	Anifrolumab 300 mg v Placebo
Number of subjects included in analysis	364
Analysis specification	Pre-specified
Analysis type	superiority[14]
P-value	= 0.515 [15]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportions
Point estimate	3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.7
upper limit	13.4

Notes:

[14] - The difference in estimates and associated 95% CI are weighted and are calculated using a stratified Cochran-Mantel-Haenszel (CMH) approach, with stratification factors (SLEDAI-2K score at screening [<10 points vs >= 10 points], Week 0 OCS dose [<10 mg/day vs >=10 mg/day prednisone or equivalent] and type I IFN gene signature test result at screening [high vs low]).
[15] - Nominal p-value

Post-hoc: Number of Participants Who Met the Criteria for British Isles Lupus Assessment Group-based Composite Lupus Assessment (BICLA) Response (Post-Hoc Analysis with Revised Restricted Medication Rules)

End point title	Number of Participants Who Met the Criteria for British Isles Lupus Assessment Group-based Composite Lupus Assessment (BICLA) Response (Post-Hoc Analysis with Revised Restricted Medication Rules)

End point description:

A BICLA responder was achieved if all of the following criteria was met:

All criteria related to SRI(4) (please see primary endpoint) plus:
Reduction of all baseline BILAG-2004 A to B/C/D and baseline BILAG-2004 B to C/D, and no BILAG-2004 worsening in other organ systems, as defined by 1 or more BILAG-2004 A or 1 or more new BILAG-2004 B item
No discontinuation of investigational product and no use of restricted medications beyond the revised post-hoc analysis threshold before assessment.

Rules regarding use of NSAIDS (criteria used to define participants as non-responders) were not implemented as intended per protocol and were not appropriate based on clinical practice (participant taking NSAIDs deemed as non-responder). Revised rules were designed to be more clinically appropriate, capture intent of protocol, minimize the risk of restricted medications confounding efficacy, and to allow appropriate quantification and interpretation of the relevant endpoints

End point type	Post-hoc

End point timeframe:

Week 52

End point values	Anifrolumab 150 mg	Anifrolumab 300 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	93	180	184	
Units: Participants	35	83	54	

Statistical analyses

Statistical analysis title	Analysis of Treatment Difference

Statistical analysis description:

The difference in estimates and associated 95% CI are weighted and are calculated using a stratified Cochran-Mantel-Haenszel (CMH) approach, with stratification factors (SLEDAI-2K score at screening [<10 points vs >= 10 points], Week 0 OCS dose [<10 mg/day vs >=10 mg/day prednisone or equivalent] and type I IFN gene signature test result at screening [high vs low]).

Comparison groups	Anifrolumab 300 mg v Placebo
Number of subjects included in analysis	364
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in proportions
Point estimate	16.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.7
upper limit	26.2

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline to End of Trial (Maximum of 60 weeks post first dose)	
Adverse event reporting additional description:	
AEs were either spontaneously reported by the participant or reported in response to open questions, revealed by observation, or were changes from baseline/deterioration in tests and vital signs that met SAE criteria or led to IP discontinuation. Full analysis set: All participants who had received at least one dose of investigational product.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups	
Reporting group title	Anifrolumab 150 mg
Reporting group description:	
Anifrolumab (150 mg) administered via an intravenous infusion (IV) every 4 weeks for up to 48 weeks (13 doses).	
Reporting group title	Anifrolumab 300 mg
Reporting group description:	
Anifrolumab (300 mg) administered via an intravenous infusion (IV) every 4 weeks for up to 48 weeks (13 doses).	
Reporting group title	Placebo
Reporting group description:	
Matching placebo administered via an intravenous infusion (IV) every 4 weeks for up to 48 weeks (13 doses)	

Serious adverse events	Anifrolumab 150 mg	Anifrolumab 300 mg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 93 (10.75%)	27 / 180 (15.00%)	35 / 184 (19.02%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (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
Invasive breast carcinoma			
subjects affected / exposed	1 / 93 (1.08%)	0 / 180 (0.00%)	0 / 184 (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
Invasive ductal breast carcinoma			

subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (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
Haemangioma of liver			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Raynaud's phenomenon			
subjects affected / exposed	1 / 93 (1.08%)	0 / 180 (0.00%)	0 / 184 (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
Deep vein thrombosis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis limb			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 93 (0.00%)	2 / 180 (1.11%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pain			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 93 (1.08%)	0 / 180 (0.00%)	0 / 184 (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
Food allergy			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Endometrial hypertrophy			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 93 (0.00%)	2 / 180 (1.11%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (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
Dyspnoea			

subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (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
Pulmonary embolism			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Conversion disorder			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (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
Suicide attempt			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Weight decreased			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (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
Injury, poisoning and procedural complications			
Facial bones fracture			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (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

Post procedural complication			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (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
Perirenal haematoma			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haematoma			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 93 (1.08%)	0 / 180 (0.00%)	0 / 184 (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
Angina unstable			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (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
Coronary artery disease			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (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
Myocardial infarction			

subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (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
Atrial fibrillation			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	2 / 184 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular arrhythmia			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Myasthenia gravis			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (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
Seizure			
subjects affected / exposed	1 / 93 (1.08%)	0 / 180 (0.00%)	0 / 184 (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
Syncope			

subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropsychiatric lupus			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (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
Anaemia			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Ulcerative keratitis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (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
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (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

Small intestinal obstruction			
subjects affected / exposed	1 / 93 (1.08%)	0 / 180 (0.00%)	0 / 184 (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
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug eruption			
subjects affected / exposed	1 / 93 (1.08%)	0 / 180 (0.00%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Swelling face			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephritis			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (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
Chronic kidney disease			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysuria			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Lupus nephritis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	2 / 184 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
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			
Systemic lupus erythematosus			
subjects affected / exposed	2 / 93 (2.15%)	4 / 180 (2.22%)	5 / 184 (2.72%)
occurrences causally related to treatment / all	0 / 3	0 / 6	1 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture pain			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (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
Musculoskeletal chest pain			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 93 (1.08%)	3 / 180 (1.67%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	1 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 93 (1.08%)	1 / 180 (0.56%)	2 / 184 (1.09%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appenicitis			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (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

Bronchitis			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (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
Gangrene			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 93 (1.08%)	0 / 180 (0.00%)	0 / 184 (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
Gastroenteritis			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Genital herpes			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis viral			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (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
Pyelonephritis acute			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (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
Sepsis			
subjects affected / exposed	1 / 93 (1.08%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Subcutaneous abscess			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (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
Encephalitis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Epididymitis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious colitis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella infection			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media chronic			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic infection			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			

subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 93 (0.00%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	0 / 184 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Anifrolumab 150 mg	Anifrolumab 300 mg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	78 / 93 (83.87%)	157 / 180 (87.22%)	141 / 184 (76.63%)
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 93 (5.38%)	4 / 180 (2.22%)	9 / 184 (4.89%)
occurrences (all)	5	4	11
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 93 (4.30%)	5 / 180 (2.78%)	4 / 184 (2.17%)
occurrences (all)	5	8	5
Chest pain			

subjects affected / exposed	1 / 93 (1.08%)	3 / 180 (1.67%)	0 / 184 (0.00%)
occurrences (all)	1	3	0
Non-cardiac chest pain			
subjects affected / exposed	3 / 93 (3.23%)	1 / 180 (0.56%)	5 / 184 (2.72%)
occurrences (all)	3	1	6
Fatigue			
subjects affected / exposed	0 / 93 (0.00%)	4 / 180 (2.22%)	2 / 184 (1.09%)
occurrences (all)	0	5	2
Oedema peripheral			
subjects affected / exposed	2 / 93 (2.15%)	2 / 180 (1.11%)	3 / 184 (1.63%)
occurrences (all)	2	2	3
Peripheral swelling			
subjects affected / exposed	2 / 93 (2.15%)	1 / 180 (0.56%)	1 / 184 (0.54%)
occurrences (all)	2	1	1
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	4 / 93 (4.30%)	11 / 180 (6.11%)	2 / 184 (1.09%)
occurrences (all)	6	12	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 93 (2.15%)	11 / 180 (6.11%)	7 / 184 (3.80%)
occurrences (all)	2	13	9
Epistaxis			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	5 / 184 (2.72%)
occurrences (all)	0	1	7
Psychiatric disorders			
Depression			
subjects affected / exposed	7 / 93 (7.53%)	6 / 180 (3.33%)	5 / 184 (2.72%)
occurrences (all)	7	8	5
Anxiety			
subjects affected / exposed	4 / 93 (4.30%)	4 / 180 (2.22%)	4 / 184 (2.17%)
occurrences (all)	4	5	5
Insomnia			
subjects affected / exposed	3 / 93 (3.23%)	4 / 180 (2.22%)	8 / 184 (4.35%)
occurrences (all)	3	4	9
Investigations			

Blood pressure increased			
subjects affected / exposed	2 / 93 (2.15%)	2 / 180 (1.11%)	0 / 184 (0.00%)
occurrences (all)	2	3	0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	9 / 93 (9.68%)	16 / 180 (8.89%)	13 / 184 (7.07%)
occurrences (all)	17	37	32
Contusion			
subjects affected / exposed	2 / 93 (2.15%)	4 / 180 (2.22%)	3 / 184 (1.63%)
occurrences (all)	2	4	3
Fall			
subjects affected / exposed	0 / 93 (0.00%)	6 / 180 (3.33%)	4 / 184 (2.17%)
occurrences (all)	0	7	4
Arthropod bite			
subjects affected / exposed	0 / 93 (0.00%)	4 / 180 (2.22%)	3 / 184 (1.63%)
occurrences (all)	0	4	3
Rib fracture			
subjects affected / exposed	2 / 93 (2.15%)	1 / 180 (0.56%)	1 / 184 (0.54%)
occurrences (all)	2	1	1
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 93 (6.45%)	17 / 180 (9.44%)	18 / 184 (9.78%)
occurrences (all)	8	37	23
Migraine			
subjects affected / exposed	4 / 93 (4.30%)	5 / 180 (2.78%)	5 / 184 (2.72%)
occurrences (all)	4	6	6
Dizziness			
subjects affected / exposed	2 / 93 (2.15%)	5 / 180 (2.78%)	7 / 184 (3.80%)
occurrences (all)	2	5	8
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	1 / 93 (1.08%)	4 / 180 (2.22%)	3 / 184 (1.63%)
occurrences (all)	1	4	3
Anaemia			
subjects affected / exposed	0 / 93 (0.00%)	1 / 180 (0.56%)	4 / 184 (2.17%)
occurrences (all)	0	1	4

Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	2 / 93 (2.15%)	2 / 180 (1.11%)	1 / 184 (0.54%)
occurrences (all)	2	2	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	8 / 93 (8.60%)	6 / 180 (3.33%)	14 / 184 (7.61%)
occurrences (all)	11	9	14
Vomiting			
subjects affected / exposed	4 / 93 (4.30%)	9 / 180 (5.00%)	4 / 184 (2.17%)
occurrences (all)	7	9	6
Nausea			
subjects affected / exposed	3 / 93 (3.23%)	9 / 180 (5.00%)	14 / 184 (7.61%)
occurrences (all)	5	10	19
Gastrooesophageal reflux disease			
subjects affected / exposed	4 / 93 (4.30%)	5 / 180 (2.78%)	6 / 184 (3.26%)
occurrences (all)	4	5	6
Dyspepsia			
subjects affected / exposed	6 / 93 (6.45%)	3 / 180 (1.67%)	5 / 184 (2.72%)
occurrences (all)	6	6	5
Abdominal pain			
subjects affected / exposed	2 / 93 (2.15%)	4 / 180 (2.22%)	2 / 184 (1.09%)
occurrences (all)	2	6	2
Abdominal pain upper			
subjects affected / exposed	1 / 93 (1.08%)	4 / 180 (2.22%)	8 / 184 (4.35%)
occurrences (all)	1	5	11
Constipation			
subjects affected / exposed	1 / 93 (1.08%)	4 / 180 (2.22%)	2 / 184 (1.09%)
occurrences (all)	1	4	2
Abdominal distension			
subjects affected / exposed	2 / 93 (2.15%)	0 / 180 (0.00%)	0 / 184 (0.00%)
occurrences (all)	2	0	0
Gastritis			
subjects affected / exposed	1 / 93 (1.08%)	1 / 180 (0.56%)	5 / 184 (2.72%)
occurrences (all)	1	1	5
Skin and subcutaneous tissue disorders			

Rash pruritic			
subjects affected / exposed	3 / 93 (3.23%)	0 / 180 (0.00%)	1 / 184 (0.54%)
occurrences (all)	3	0	1
Rash			
subjects affected / exposed	1 / 93 (1.08%)	0 / 180 (0.00%)	5 / 184 (2.72%)
occurrences (all)	1	0	5
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 93 (0.00%)	4 / 180 (2.22%)	0 / 184 (0.00%)
occurrences (all)	0	5	0
Endocrine disorders			
Steroid withdrawal syndrome			
subjects affected / exposed	0 / 93 (0.00%)	5 / 180 (2.78%)	1 / 184 (0.54%)
occurrences (all)	0	5	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 93 (2.15%)	11 / 180 (6.11%)	3 / 184 (1.63%)
occurrences (all)	3	13	5
Back pain			
subjects affected / exposed	2 / 93 (2.15%)	10 / 180 (5.56%)	13 / 184 (7.07%)
occurrences (all)	2	10	16
Fibromyalgia			
subjects affected / exposed	3 / 93 (3.23%)	2 / 180 (1.11%)	4 / 184 (2.17%)
occurrences (all)	3	2	4
Pain in extremity			
subjects affected / exposed	3 / 93 (3.23%)	2 / 180 (1.11%)	1 / 184 (0.54%)
occurrences (all)	3	2	1
Myalgia			
subjects affected / exposed	2 / 93 (2.15%)	2 / 180 (1.11%)	5 / 184 (2.72%)
occurrences (all)	3	2	6
Osteoarthritis			
subjects affected / exposed	3 / 93 (3.23%)	1 / 180 (0.56%)	1 / 184 (0.54%)
occurrences (all)	4	1	1
Trigger finger			
subjects affected / exposed	2 / 93 (2.15%)	0 / 180 (0.00%)	0 / 184 (0.00%)
occurrences (all)	2	0	0

Bursitis			
subjects affected / exposed	1 / 93 (1.08%)	0 / 180 (0.00%)	4 / 184 (2.17%)
occurrences (all)	1	0	5
Muscle spasms			
subjects affected / exposed	1 / 93 (1.08%)	1 / 180 (0.56%)	4 / 184 (2.17%)
occurrences (all)	1	1	4
Osteoporosis			
subjects affected / exposed	1 / 93 (1.08%)	0 / 180 (0.00%)	4 / 184 (2.17%)
occurrences (all)	1	0	4
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	15 / 93 (16.13%)	36 / 180 (20.00%)	24 / 184 (13.04%)
occurrences (all)	18	58	28
Upper respiratory tract infection			
subjects affected / exposed	17 / 93 (18.28%)	22 / 180 (12.22%)	19 / 184 (10.33%)
occurrences (all)	25	27	27
Urinary tract infection			
subjects affected / exposed	8 / 93 (8.60%)	22 / 180 (12.22%)	26 / 184 (14.13%)
occurrences (all)	10	29	32
Bronchitis			
subjects affected / exposed	7 / 93 (7.53%)	15 / 180 (8.33%)	9 / 184 (4.89%)
occurrences (all)	9	17	11
Pharyngitis			
subjects affected / exposed	6 / 93 (6.45%)	12 / 180 (6.67%)	13 / 184 (7.07%)
occurrences (all)	8	13	15
Herpes zoster			
subjects affected / exposed	5 / 93 (5.38%)	10 / 180 (5.56%)	3 / 184 (1.63%)
occurrences (all)	5	10	3
Sinusitis			
subjects affected / exposed	5 / 93 (5.38%)	8 / 180 (4.44%)	12 / 184 (6.52%)
occurrences (all)	6	12	13
Pneumonia			
subjects affected / exposed	4 / 93 (4.30%)	4 / 180 (2.22%)	2 / 184 (1.09%)
occurrences (all)	5	4	2
Gastroenteritis			

subjects affected / exposed	5 / 93 (5.38%)	5 / 180 (2.78%)	2 / 184 (1.09%)
occurrences (all)	5	5	3
Oral herpes			
subjects affected / exposed	0 / 93 (0.00%)	8 / 180 (4.44%)	5 / 184 (2.72%)
occurrences (all)	0	10	8
Cellulitis			
subjects affected / exposed	0 / 93 (0.00%)	6 / 180 (3.33%)	2 / 184 (1.09%)
occurrences (all)	0	6	2
Folliculitis			
subjects affected / exposed	4 / 93 (4.30%)	3 / 180 (1.67%)	3 / 184 (1.63%)
occurrences (all)	5	4	3
Conjunctivitis			
subjects affected / exposed	2 / 93 (2.15%)	4 / 180 (2.22%)	1 / 184 (0.54%)
occurrences (all)	2	5	1
Influenza			
subjects affected / exposed	2 / 93 (2.15%)	3 / 180 (1.67%)	2 / 184 (1.09%)
occurrences (all)	2	3	2
Respiratory tract infection			
subjects affected / exposed	0 / 93 (0.00%)	5 / 180 (2.78%)	3 / 184 (1.63%)
occurrences (all)	0	7	3
Rhinitis			
subjects affected / exposed	1 / 93 (1.08%)	4 / 180 (2.22%)	4 / 184 (2.17%)
occurrences (all)	1	9	4
Tooth infection			
subjects affected / exposed	0 / 93 (0.00%)	5 / 180 (2.78%)	0 / 184 (0.00%)
occurrences (all)	0	5	0
Vulvovaginal mycotic infection			
subjects affected / exposed	2 / 93 (2.15%)	3 / 180 (1.67%)	4 / 184 (2.17%)
occurrences (all)	2	3	4
Onychomycosis			
subjects affected / exposed	0 / 93 (0.00%)	4 / 180 (2.22%)	0 / 184 (0.00%)
occurrences (all)	0	4	0
Subcutaneous abscess			
subjects affected / exposed	2 / 93 (2.15%)	1 / 180 (0.56%)	1 / 184 (0.54%)
occurrences (all)	2	1	1
Furuncle			

subjects affected / exposed	2 / 93 (2.15%)	1 / 180 (0.56%)	1 / 184 (0.54%)
occurrences (all)	3	1	1
Viral infection			
subjects affected / exposed	2 / 93 (2.15%)	1 / 180 (0.56%)	2 / 184 (1.09%)
occurrences (all)	2	1	4
Cystitis			
subjects affected / exposed	1 / 93 (1.08%)	1 / 180 (0.56%)	4 / 184 (2.17%)
occurrences (all)	1	1	4
Hordeolum			
subjects affected / exposed	2 / 93 (2.15%)	0 / 180 (0.00%)	0 / 184 (0.00%)
occurrences (all)	2	0	0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	3 / 93 (3.23%)	1 / 180 (0.56%)	4 / 184 (2.17%)
occurrences (all)	4	1	5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 February 2016	HIV testing was added as a screening assessment.
23 March 2016	The washout periods for certain restricted medications including anakinra, apremilast, atacicept (TACI-Ig), belimumab, and blisibimod (AMG 623) were corrected.
18 May 2016	Inclusion and exclusion criteria was clarified. Long term extension (LTE) was also clarified.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported