



Clinical trial results:

A Phase 2, Randomized Study to Evaluate the Efficacy and Safety of MEDI-546 in Subjects with Systemic Lupus Erythematosus

Summary

EudraCT number	2011-004296-36
Trial protocol	CZ HU BG
Global end of trial date	08 April 2015

Results information

Result version number	v2 (current)
This version publication date	22 October 2016
First version publication date	23 July 2016
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	CD-IA-MEDI-546-1013
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01438489
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	MedImmune, LLC
Sponsor organisation address	Milstein Building, Granta Park, Cambridge, United Kingdom, CB21 6GH
Public contact	Gabor Illei, MD, Senior Director, MedImmune, LLC, +44 3013980000, illeig@Medimmune.com
Scientific contact	Gabor Illei, MD, Senior Director, MedImmune, LLC, +44 3013980000, illeig@Medimmune.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 June 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	08 April 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the efficacy of anifrolumab compared to placebo at Day 169 (Week 24) in subjects with chronic, moderately to severely active systemic lupus erythematosus (SLE) with an inadequate response to standard of care treatment for SLE.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Participating participant signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy:

Participants received background therapy with at least one of the following: oral corticosteroids, antimalarials, azathioprine, methotrexate or mycophenolate. Tapering of oral corticosteroids was allowed after randomization; all other background treatments were continued at stable doses.

Evidence for comparator: -

Actual start date of recruitment	20 January 2012
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	Brazil: 3
Country: Number of subjects enrolled	Bulgaria: 9
Country: Number of subjects enrolled	Colombia: 44
Country: Number of subjects enrolled	Czech Republic: 3
Country: Number of subjects enrolled	Hungary: 10
Country: Number of subjects enrolled	India: 3
Country: Number of subjects enrolled	Mexico: 16
Country: Number of subjects enrolled	Peru: 50
Country: Number of subjects enrolled	Poland: 32
Country: Number of subjects enrolled	Romania: 2
Country: Number of subjects enrolled	Korea, Republic of: 6
Country: Number of subjects enrolled	Taiwan: 12
Country: Number of subjects enrolled	Ukraine: 22
Country: Number of subjects enrolled	United States: 95

Worldwide total number of subjects	307
EEA total number of subjects	56

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)	307
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 626 participants were screened out of which 319 participants did not meet eligibility criteria and were considered screen failures, and 307 participants were randomized into the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received placebo matched to anifrolumab intravenous (IV) infusion every 4 weeks for 48 weeks.

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:

Participants received placebo matched to anifrolumab intravenous (IV) infusion every 4 weeks for 48 weeks.

Arm title	Anifrolumab 300 mg
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Arm description:

Participants received 300 milligram (mg) anifrolumab as an intravenous infusion every 4 weeks for 48 weeks.

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

Dosage and administration details:

Participants received 300 milligram (mg) anifrolumab as an intravenous infusion every 4 weeks for 48 weeks.

Arm title	Anifrolumab 1000 mg
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Arm description:

Participants received 1000 mg anifrolumab as an intravenous infusion every 4 weeks for 48 weeks.

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

Dosage and administration details:

Participants received 300 milligram (mg) anifrolumab as an intravenous infusion every 4 weeks for 48 weeks.

Number of subjects in period 1	Placebo	Anifrolumab 300 mg	Anifrolumab 1000 mg
Started	103	100	104
Completed	77	84	85
Not completed	26	16	19
Adverse event, serious fatal	-	-	1
Consent withdrawn by subject	11	3	8
Subject choice/Subject moved	2	1	1
Did not complete all 3 follow-up visits	2	5	2
Inadequate venous access	-	2	-
Received prohibited medication	1	-	-
Investigator decision	-	1	-
Lost to follow-up	4	2	2
Sponsor decision	4	1	4
AE/SAEs	2	1	1

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description: Participants received placebo matched to anifrolumab intravenous (IV) infusion every 4 weeks for 48 weeks.	
Reporting group title	Anifrolumab 300 mg
Reporting group description: Participants received 300 milligram (mg) anifrolumab as an intravenous infusion every 4 weeks for 48 weeks.	
Reporting group title	Anifrolumab 1000 mg
Reporting group description: Participants received 1000 mg anifrolumab as an intravenous infusion every 4 weeks for 48 weeks.	

Reporting group values	Placebo	Anifrolumab 300 mg	Anifrolumab 1000 mg
Number of subjects	103	100	104
Age categorical Units: Subjects			
Adults (18-64 years)	103	100	104
Age Continuous Units: Years			
arithmetic mean	39.2	39.3	40.8
standard deviation	± 12.9	± 12	± 11.6
Gender, Male/Female Units: Participants			
Male	9	6	5
Female	94	94	99
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaskan Native	0	4	1
Asian	13	3	6
Black or African American	12	19	10
Native Hawaiian or Other Pacific Islander	0	0	0
White	41	36	51
Other	36	37	36
Multiple category checked	1	1	0
Region of Enrollment Units: Subjects			
BRAZIL	3	0	0
BULGARIA	3	2	4
COLOMBIA	16	10	18
CZECH REPUBLIC	1	0	2
HUNGARY	2	5	3
INDIA	2	1	0
MEXICO	4	7	5
PERU	15	22	13
POLAND	11	9	12

ROMANIA	1	0	1
SOUTH KOREA	3	0	3
TAIWAN	7	2	3
UKRAINE	7	4	11
UNITED STATES OF AMERICA	28	38	29
Study Specific Characteristics			
Units: Kilogram			
arithmetic mean	68.08	69.62	70.74
standard deviation	± 18.98	± 17.09	± 17.29

Reporting group values	Total		
Number of subjects	307		
Age categorical			
Units: Subjects			
Adults (18-64 years)	307		
Age Continuous			
Units: Years			
arithmetic mean			
standard deviation	-		
Gender, Male/Female			
Units: Participants			
Male	20		
Female	287		
Race/Ethnicity, Customized			
Units: Subjects			
American Indian or Alaskan Native	5		
Asian	22		
Black or African American	41		
Native Hawaiian or Other Pacific Islander	0		
White	128		
Other	109		
Multiple category checked	2		
Region of Enrollment			
Units: Subjects			
BRAZIL	3		
BULGARIA	9		
COLOMBIA	44		
CZECH REPUBLIC	3		
HUNGARY	10		
INDIA	3		
MEXICO	16		
PERU	50		
POLAND	32		
ROMANIA	2		
SOUTH KOREA	6		
TAIWAN	12		
UKRAINE	22		
UNITED STATES OF AMERICA	95		

Study Specific Characteristics Units: Kilogram arithmetic mean standard deviation	-		
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Subject analysis sets

Subject analysis set title	Placebo
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received placebo matched to anifrolumab intravenous (IV) infusion every 4 weeks for 48 weeks. One participant from Placebo group received Anifrolumab 1000 mg once in the study and hence, included it in the Anifrolumab 1000 mg group. This subject analysis set is created as per Safety population. The Safety population included all participants who received any dose of investigational product.

Subject analysis set title	Anifrolumab 300 mg
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received 300 milligram (mg) anifrolumab as an intravenous infusion every 4 weeks for 48 weeks. This subject analysis set is created as per Safety population. The Safety population included all participants who received any dose of investigational product.

Subject analysis set title	Anifrolumab 1000 mg
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received 1000 mg anifrolumab as an intravenous infusion every 4 weeks for 48 weeks. One participant from Placebo group received Anifrolumab 1000 mg once in the study and hence, included it in the Anifrolumab 1000 mg group. This subject analysis set is created as per Safety population. The Safety population included all participants who received any dose of investigational product.

Reporting group values	Placebo	Anifrolumab 300 mg	Anifrolumab 1000 mg
Number of subjects	101	99	105
Age categorical Units: Subjects			
Adults (18-64 years)	101	99	105
Age Continuous Units: Years			
arithmetic mean	39.4	39.1	40.6
standard deviation	± 12.9	± 11.9	± 11.6
Gender, Male/Female Units: Participants			
Male	9	6	5
Female	92	93	100
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaskan Native	0	4	1
Asian	13	3	6
Black or African American	11	19	11
Native Hawaiian or Other Pacific Islander	0	0	0
White	41	35	51
Other	35	37	36
Multiple category checked	1	1	0
Region of Enrollment Units: Subjects			

BRAZIL BULGARIA COLOMBIA CZECH REPUBLIC HUNGARY INDIA MEXICO PERU POLAND ROMANIA SOUTH KOREA TAIWAN UKRAINE UNITED STATES OF AMERICA			
Study Specific Characteristics			
Units: Kilogram			
arithmetic mean	67.66	69.54	71.17
standard deviation	± 18.56	± 17.15	± 17.76

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Participants received placebo matched to anifrolumab intravenous (IV) infusion every 4 weeks for 48 weeks.	
Reporting group title	Anifrolumab 300 mg
Reporting group description: Participants received 300 milligram (mg) anifrolumab as an intravenous infusion every 4 weeks for 48 weeks.	
Reporting group title	Anifrolumab 1000 mg
Reporting group description: Participants received 1000 mg anifrolumab as an intravenous infusion every 4 weeks for 48 weeks.	
Subject analysis set title	Placebo
Subject analysis set type	Safety analysis
Subject analysis set description: Participants received placebo matched to anifrolumab intravenous (IV) infusion every 4 weeks for 48 weeks. One participant from Placebo group received Anifrolumab 1000 mg once in the study and hence, included it in the Anifrolumab 1000 mg group. This subject analysis set is created as per Safety population. The Safety population included all participants who received any dose of investigational product.	
Subject analysis set title	Anifrolumab 300 mg
Subject analysis set type	Safety analysis
Subject analysis set description: Participants received 300 milligram (mg) anifrolumab as an intravenous infusion every 4 weeks for 48 weeks. This subject analysis set is created as per Safety population. The Safety population included all participants who received any dose of investigational product.	
Subject analysis set title	Anifrolumab 1000 mg
Subject analysis set type	Safety analysis
Subject analysis set description: Participants received 1000 mg anifrolumab as an intravenous infusion every 4 weeks for 48 weeks. One participant from Placebo group received Anifrolumab 1000 mg once in the study and hence, included it in the Anifrolumab 1000 mg group. This subject analysis set is created as per Safety population. The Safety population included all participants who received any dose of investigational product.	

Primary: Percentage of Participants Achieving an Systemic Lupus Erythematosus (SLE) Responder Index [SRI (4)] Response With Oral Corticosteroids (OCS) Tapering at Day 169

End point title	Percentage of Participants Achieving an Systemic Lupus Erythematosus (SLE) Responder Index [SRI (4)] Response With Oral Corticosteroids (OCS) Tapering at Day 169
End point description: An SRI (4) responder defined as participant who had 1) reduction in baseline Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score of greater than or equal to (\geq) 4 points; 2) no worsening of disease from baseline as measured by Physician Global Assessment (MDGA) (worsening was defined as an increase of ≥ 0.3 from baseline on 0 to 3.0 visual analog scale); 3) no new British Isles Lupus Assessment Group 2004 (BILAG-2004) Index 'A' organ system score and no more than one new or worsening BILAG-2004 Index 'B' organ system score. OCS tapering requires a sustained reduction of OCS from Day 85 through Day 169 [less than 10 milligram per day (mg/day) and less or equal to dose received on Day 1]. SRI was analyzed by logistic regression model. The modified Intent-To-Treat (mITT) included all randomized participants who received any investigational product and had a baseline primary efficacy measurement. Here, "N" signifies evaluable participants for this outcome measure.	
End point type	Primary
End point timeframe: Day 169	

End point values	Placebo	Anifrolumab 300 mg	Anifrolumab 1000 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	99	104	
Units: Percentage of Participants				
number (not applicable)	17.6	34.3	28.8	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
All-comers	
Comparison groups	Placebo v Anifrolumab 300 mg
Number of subjects included in analysis	201
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.014
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.38
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.33
upper limit	4.26

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
All-comers	
Comparison groups	Placebo v Anifrolumab 1000 mg
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.063
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.94
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.08
upper limit	3.49

Primary: Percentage of Type I Interferon (IFN) Test High Participants Achieving an Systemic Lupus Erythematosus Responder Index (SRI) (4) Response With Oral Corticosteroids (OCS) Tapering at Day 169

End point title	Percentage of Type I Interferon (IFN) Test High Participants Achieving an Systemic Lupus Erythematosus Responder Index (SRI) (4) Response With Oral Corticosteroids (OCS) Tapering at Day 169
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End point description:

Type I IFN signature in whole blood assessed by using a 4-gene diagnostic test. Blood samples collected were used to identify participants as IFN test-high. Results of this test were used to stratify participants. An SRI (4) Responder were participant who had 1) a reduction in baseline SLEDAI-2K disease activity score of ≥ 4 points; 2) no worsening of disease from baseline as measured by Physician Global Assessment (MDGA) (worsening was defined as an increase of ≥ 0.3 from baseline on 0 to 3.0 visual analog scale); 3) no new BILAG-2004 Index A organ system score and no more than one new or worsening BILAG-2004 Index B organ system score. OCS tapering requires a sustained reduction of OCS from Day 85 through Day 169 [less than 10 mg/day and less or equal to the dose received on Day 1]. mITT included all randomized participants who received any investigational product and had baseline primary efficacy measurement. Here, "N" signifies evaluable participants for this outcome measure.

End point type	Primary
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End point timeframe:

Day 169

End point values	Placebo	Anifrolumab 300 mg	Anifrolumab 1000 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	75	78	
Units: Percentage of Participants				
number (not applicable)	13.2	36	28.2	

Statistical analyses

Statistical analysis title	Statistical Analysis 2
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Statistical analysis description:

High

Comparison groups	Placebo v Anifrolumab 1000 mg
Number of subjects included in analysis	154
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.029
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.65
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.27
upper limit	5.53

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: High	
Comparison groups	Placebo v Anifrolumab 300 mg
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.004
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.55
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.72
upper limit	7.32

Secondary: Percentage of Participants Achieving an Systemic Lupus Erythematosus (SLE) Responder Index [SRI (4)] Response With Oral Corticosteroids (OCS) Tapering at Day 365

End point title	Percentage of Participants Achieving an Systemic Lupus Erythematosus (SLE) Responder Index [SRI (4)] Response With Oral Corticosteroids (OCS) Tapering at Day 365
End point description: An SRI (4) Responder was defined as a participant who had 1) a reduction in baseline SLEDAI-2K disease activity score of ≥ 4 points; 2) no worsening of disease from baseline as measured by the MDGA (worsening was defined as an increase of ≥ 0.3 from baseline on a 0 to 3.0 visual analog scale); and 3) no new British Isles Lupus Assessment Group 2004 (BILAG-2004) Index A organ system score and no more than one new or worsening BILAG-2004 Index B organ system score. OCS tapering requires a sustained reduction of OCS from Day 281 through Day 365 (less than 10 mg/day and less or equal to the dose received on Day 1). SRI was analyzed by a logistic regression model. The mITT population included all randomized participants who received any investigational product and had a baseline primary efficacy measurement. Here, "N" signifies evaluable participants for this outcome measure.	
End point type	Secondary
End point timeframe: Day 365	

End point values	Placebo	Anifrolumab 300 mg	Anifrolumab 1000 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	99	104	
Units: Percentage of Participants				
number (not applicable)	25.5	51.5	38.5	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants on Oral Corticosteroids (OCS) ≥ 10 mg/day of Prednisone or Equivalent at Baseline who Were able to Taper to less than or equal to (\leq) 7.5 mg/day at Day 365

End point title	Percentage of Participants on Oral Corticosteroids (OCS) ≥ 10 mg/day of Prednisone or Equivalent at Baseline who Were able to Taper to less than or equal to (\leq) 7.5 mg/day at Day 365
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End point description:

Participants on OCS ≥ 10 mg/day of prednisone or equivalent at baseline who were able to taper to ≤ 7.5 mg/day at Day 365 were evaluated. The mITT population included all randomized participants who received any investigational product and had a baseline primary efficacy measurement. Here, "N" signifies evaluable participants for this outcome measure.

End point type	Secondary
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End point timeframe:

Day 365

End point values	Placebo	Anifrolumab 300 mg	Anifrolumab 1000 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	64	55	63	
Units: Percentage of Participants				
number (not applicable)	26.6	56.4	31.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Adverse Events of Special Interest (AESIs) and Treatment-Emergent Serious Adverse Events (TESAEs)

End point title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Adverse Events of Special Interest (AESIs) and Treatment-Emergent Serious Adverse Events (TESAEs)
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End point description:

An adverse event (AE) was any untoward medical occurrence in a study participant administered a pharmaceutical product and which does not necessarily have a causal relationship with treatment. A serious AE (SAE) was an AE resulting in any of following outcomes or deemed significant for any other reason: death; initial/prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly (in offspring of participant). AEs may be treatment emergent (TE) [that is, occurring after initial receipt of investigational product] or non-TE. An AESI is one of scientific and medical concern specific to understanding biologics and requires close monitoring and rapid communication by investigator to sponsor. The safety population included

participants who received any investigational product. Here, "N" signifies evaluable participants for this outcome measure.

End point type	Secondary
End point timeframe:	
Day 1 (Baseline) to Day 422 (End of Study)	

End point values	Placebo	Anifrolumab 300 mg	Anifrolumab 1000 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	101	99	105	
Units: Participants				
TEAEs	78	84	90	
TESAEs	19	16	18	
AESIs	12	10	15	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Significant Laboratory Abnormalities in Investigations Reported as Treatment-Emergent Adverse Events

End point title	Number of Participants With Clinically Significant Laboratory Abnormalities in Investigations Reported as Treatment-Emergent Adverse Events
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End point description:

Any medically significant change in laboratory evaluations were recorded as Treatment emergent adverse events. The safety population included participants who received any investigational product. Here, "N" signifies evaluable participants for this outcome measure. One participant from Placebo group received Anifrolumab 1000 mg once and hence, included it in the Anifrolumab 1000 mg group.

End point type	Secondary
End point timeframe:	
Day 1 (Baseline) to Day 422 (End of Study)	

End point values	Placebo	Anifrolumab 300 mg	Anifrolumab 1000 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	101	99	105	
Units: Participants				
Neutrophil count increased	0	1	3	
Leukocytosis	0	1	2	
Leukopenia	2	0	3	
Neutropenia	0	0	3	
Anaemia	0	0	2	
Iron deficiency anaemia	0	1	1	
Lymphopenia	0	0	2	
Microcytic anaemia	1	0	2	

Thrombocytosis	0	1	0	
White blood cell count increased	0	0	1	
Monocyte count increased	0	0	1	
Hypochromic anaemia	1	0	0	
Hyperglycaemia	1	3	1	
Hypokalaemia	2	3	0	
Hepatic enzyme increased	1	0	3	
Hypocalcaemia	0	1	1	
Lipid metabolism disorder	0	1	1	
Alanine aminotransferase increased	0	1	1	
Aspartate aminotransferase increased	0	2	0	
Blood creatine phosphokinase increased	0	1	1	
Hyperlipidaemia	1	0	1	
Hypertriglyceridaemia	2	1	0	
Hyponatraemia	0	0	1	
Blood alkaline phosphatase increased	0	1	0	
Gamma-glutamyltransferase increased	0	1	0	
Glomerular filtration rate decreased	0	1	0	
Transaminases increased	1	0	1	
Dyslipidaemia	1	0	0	
Alanine aminotransferase abnormal	1	0	0	
Aspartate aminotransferase abnormal	1	0	0	
Blood triglycerides abnormal	1	0	0	
Glomerular filtration rate increased	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Vital Signs Abnormalities Reported as Treatment-Emergent Adverse Events (TEAEs)

End point title	Number of Participants With Vital Signs Abnormalities Reported as Treatment-Emergent Adverse Events (TEAEs)
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End point description:

Vital sign parameters are temperature, blood pressure, respiratory rate, heart rate and weight. Vital signs abnormalities were reported as TEAEs. The safety population included participants who received any investigational product. Here, "N" signifies evaluable participants for this outcome measure. One participant from Placebo group received Anifrolumab 1000 mg once and hence, included it in the Anifrolumab 1000 mg group.

End point type	Secondary
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End point timeframe:

Day 1 (Baseline) to Day 422 (End of Study)

End point values	Placebo	Anifrolumab 300 mg	Anifrolumab 1000 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	101	99	105	
Units: Participants				
Hypertension	7	3	2	
Pyrexia	5	0	3	
Blood pressure increased	0	2	1	
Blood pressure decreased	0	0	1	
Hypotension	0	1	0	
Secondary hypertension	0	0	1	
Weight increased	0	0	1	
Blood pressure abnormal	1	0	0	
Chills	1	0	0	
Hypertensive emergency	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Electrocardiogram (ECG) Abnormalities Reported as Treatment-Emergent Adverse Events (TEAEs)

End point title	Number of Participants With Electrocardiogram (ECG) Abnormalities Reported as Treatment-Emergent Adverse Events (TEAEs)
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End point description:

Any medically significant changes from the screening ECG was recorded as TEAEs. An abnormal ECG findings such as QT prolonged were reported as treatment emergent adverse events. The safety population included participants who received any investigational product. Here, "N" signifies evaluable participants for this outcome measure. One participant from Placebo group received Anifrolumab 1000 mg once and hence, included it in the Anifrolumab 1000 mg group.

End point type	Secondary
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End point timeframe:

Day 1 (Baseline) to Day 422 (End of Study)

End point values	Placebo	Anifrolumab 300 mg	Anifrolumab 1000 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	101	99	105	
Units: Participants	0	0	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of SLE Participants With Positive Anti-drug Antibody (ADA)

End point title	Percentage of SLE Participants With Positive Anti-drug Antibody (ADA)
End point description: Anti-drug antibody responses to anifrolumab in serum were evaluated. The safety population included participants who received any investigational product. Here, "N" and "n" signifies evaluable participants for this outcome measure and for specified category of the arms respectively. One participant from Placebo group received Anifrolumab 1000 mg once and hence, included it in the Anifrolumab 1000 mg group.	
End point type	Secondary
End point timeframe: Days 1, 85, 141, 169, 253, 337 (Treatment Phase), 365, 396, and 422 (Follow-up Period)	

End point values	Placebo	Anifrolumab 300 mg	Anifrolumab 1000 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	101	99	105	
Units: Percentage of Participants				
number (not applicable)				
Day 1 (n=100,98,105)	1	1	1.9	
Day 85 (n=91,93,98)	1.1	0	0	
Day 141 (n=84,94,93)	2.4	0	2.2	
Day 169 (n=81,89,92)	2.5	0	1.1	
Day 253 (n=72,86,86)	0	1.2	0	
Day 337 (n=70,87,76)	0	1.1	0	
Day 365 (n=85,96,94)	0	1	1.1	
Day 396 (n=78,88,90)	0	2.3	0	
Day 422 (n=76,86,77)	1.3	5.8	0	
Any Visit Post Baseline (n= 99,98,102)	3	5.1	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Neutralization Ratio of 21-Gene Type I Interferon (IFN) Signature for Participants With Positive Baseline Pharmacodynamic (PD) Gene Signature

End point title	Neutralization Ratio of 21-Gene Type I Interferon (IFN) Signature for Participants With Positive Baseline Pharmacodynamic (PD) Gene Signature
End point description: The PD positive and negative gene signature was determined by comparing the expression of type I IFN-inducible genes in a 21-gene panel in study participants relative to pooled normal blood collected from healthy participants. The mITT population included all randomized participants who received any investigational product and had a baseline primary efficacy measurement. Here, "N" signifies evaluable participants for this outcome measure and "n" signifies evaluable participants for the specified category of the arms respectively.	
End point type	Secondary
End point timeframe: Days 29, 85, 141, 169, 253, 337 (treatment phase), on Days 365, 396, and 422 (follow up period)	

End point values	Placebo	Anifrolumab 300 mg	Anifrolumab 1000 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	99	104	
Units: Ratio				
arithmetic mean (standard deviation)				
Day 29 (n= 68, 66, 73)	-0.753 (± 44.678)	70.194 (± 40.028)	82.056 (± 16.108)	
Day 85 (n= 63, 62, 72)	-5.412 (± 44.354)	72.639 (± 34.443)	79.35 (± 40.428)	
Day 141 (n= 59, 64, 68)	-25.411 (± 78.391)	73.662 (± 36.684)	88.569 (± 10.364)	
Day 169 (n= 56, 60, 66)	-17.122 (± 67.603)	77.364 (± 30.733)	88.126 (± 10.278)	
Day 253 (n= 50, 60, 61)	-9.908 (± 49.826)	73.972 (± 41.267)	86.099 (± 15.615)	
Day 337 (n= 49, 59, 53)	-13.784 (± 45.541)	79.363 (± 28.803)	87.811 (± 8.41)	
Day 365 (n= 58, 66, 68)	-6.428 (± 50.358)	72.796 (± 35.552)	81.115 (± 53.121)	
Day 396 (n= 56, 61, 64)	-22.106 (± 64.529)	11.51 (± 56.385)	72.291 (± 31.182)	
Day 422 (n= 53, 57, 55)	-31.777 (± 70.173)	-0.836 (± 44.596)	37.532 (± 66.339)	

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of Anifrolumab at Day 1, 169 and 337

End point title	Maximum Observed Plasma Concentration (Cmax) of Anifrolumab at Day 1, 169 and 337 ^[1]
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End point description:

Maximum plasma concentration (Cmax) was defined as the peak plasma level of anifrolumab, derived from plasma concentration -time data. The Pharmacokinetic population included all treated participants with at least 1 Pharmacokinetic assessment. Here, "N" signifies evaluable participants for this outcome measure and "n" signifies evaluable participants for the specified category of the arms respectively.

End point type	Secondary
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End point timeframe:

Pre-infusion and 15 minutes post-infusion on Day 1, 169 and 337

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analyses for this end point

End point values	Anifrolumab 300 mg	Anifrolumab 1000 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	104		
Units: micrograms/milliliter (mcg/mL)				
arithmetic mean (standard deviation)				
Day 1 (n=98,104)	82.8 (± 64.5)	248 (± 79.9)		
Day 169 (n=86,87)	110 (± 63.7)	375 (± 137)		
Day 337 (n=83,67)	127 (± 64.6)	439 (± 140)		

Statistical analyses

No statistical analyses for this end point

Secondary: Accumulation Ratio of Maximum Observed Plasma Concentration (C_{max},AR) of Anifrolumab

End point title	Accumulation Ratio of Maximum Observed Plasma Concentration (C _{max} ,AR) of Anifrolumab ^[2]
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End point description:

Accumulation ratio for maximum plasma concentration (C_{max},AR) of anifrolumab after multiple administration at Day 169 and 337 was calculated. The Pharmacokinetic population included all treated participants with at least 1 Pharmacokinetic assessment. Here, "N" signifies evaluable participants for this outcome measure and "n" signifies evaluable participants for the specified category of the arms respectively.

End point type	Secondary
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End point timeframe:

Pre-infusion and 15 minutes post-infusion on Day 169 and 337

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analyses for this end point

End point values	Anifrolumab 300 mg	Anifrolumab 1000 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	86		
Units: Ratio				
median (full range (min-max))				
Day 169 (n=81,86)	1.36 (0.0367 to 3680)	1.43 (0.211 to 191)		
Day 337 (n=78,66)	1.56 (0.132 to 7050)	1.76 (0.492 to 240)		

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Concentration (C_{trough}) of Anifrolumab at Day 29, 169 and 365

End point title	Trough Concentration (C _{trough}) of Anifrolumab at Day 29, 169 and 365 ^[3]
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End point description:

Trough concentration (C_{trough}) of anifrolumab at Day 29, 169 and 365 were calculated. The Pharmacokinetic population included all treated participants with at least 1 Pharmacokinetic assessment. Here, "N" signifies evaluable participants for this outcome measure and "n" signifies evaluable participants for the specified category of the arms respectively.

End point type	Secondary
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End point timeframe:

Pre-infusion and 15 minutes post-infusion on Day 29, 169 and 365

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analyses for this end point

End point values	Anifrolumab 300 mg	Anifrolumab 1000 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	99		
Units: microgram per milliliter				
arithmetic mean (standard deviation)				
Day 29 (n=95,99)	7.95 (± 6.17)	46.8 (± 24.6)		
Day 169 (n=87,87)	18.4 (± 12.9)	110 (± 60.5)		
Day 365 (n=83,71)	23.6 (± 15.5)	154 (± 89.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Accumulation Ratio of Trough Concentration (C_{trough},AR) of Anifrolumab at Day 169 and 365

End point title	Accumulation Ratio of Trough Concentration (C _{trough} ,AR) of Anifrolumab at Day 169 and 365 ^[4]
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End point description:

Accumulation ratio for trough concentration (C_{trough},AR) of anifrolumab after multiple administration at Day 169 and 365 was calculated. The Pharmacokinetic population included all treated participants with at least 1 Pharmacokinetic assessment. Here, "N" signifies evaluable participants for this outcome measure and "n" signifies evaluable participants for the specified category of the arms respectively.

End point type	Secondary
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End point timeframe:

Pre-infusion and 15 minutes post-infusion on Day 169 and 365

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analyses for this end point

End point values	Anifrolumab 300 mg	Anifrolumab 1000 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	86		
Units: Ratio				
median (full range (min-max))				
Day 169 (n=82,86)	2.49 (0.0599 to 1250)	2.29 (0.299 to 30.1)		

Day 365 (n=79,70)	3.06 (0.00816 to 1130)	3.02 (0.672 to 11.7)		
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Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 (Baseline) to Day 422 (End of Study)

Adverse event reporting additional description:

1 participant from placebo arm inadvertently received one dose of anifrolumab 1000 milligram (mg).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Participants received placebo matched to anifrolumab intravenous (IV) infusion every 4 weeks for 48 weeks.

Reporting group title	Anifrolumab 1000 mg
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Reporting group description:

Participants received 1000 mg anifrolumab as an intravenous infusion every 4 weeks for 48 weeks.

Reporting group title	Anifrolumab 300 mg
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Reporting group description:

Participants received 300 milligram (mg) anifrolumab as an intravenous infusion every 4 weeks for 48 weeks.

Serious adverse events	Placebo	Anifrolumab 1000 mg	Anifrolumab 300 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 101 (18.81%)	18 / 105 (17.14%)	16 / 99 (16.16%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 101 (0.00%)	0 / 105 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	0 / 101 (0.00%)	1 / 105 (0.95%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			

subjects affected / exposed	1 / 101 (0.99%)	1 / 105 (0.95%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive emergency			
subjects affected / exposed	1 / 101 (0.99%)	0 / 105 (0.00%)	0 / 99 (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
Secondary hypertension			
subjects affected / exposed	0 / 101 (0.00%)	1 / 105 (0.95%)	0 / 99 (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
Vasculitis			
subjects affected / exposed	2 / 101 (1.98%)	0 / 105 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 101 (0.99%)	3 / 105 (2.86%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 101 (0.00%)	0 / 105 (0.00%)	1 / 99 (1.01%)
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	1 / 101 (0.99%)	0 / 105 (0.00%)	0 / 99 (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			
Dyspnoea			

subjects affected / exposed	0 / 101 (0.00%)	0 / 105 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 101 (0.99%)	0 / 105 (0.00%)	0 / 99 (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
Pulmonary embolism			
subjects affected / exposed	0 / 101 (0.00%)	1 / 105 (0.95%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory disorder			
subjects affected / exposed	1 / 101 (0.99%)	0 / 105 (0.00%)	0 / 99 (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
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	0 / 101 (0.00%)	0 / 105 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Hand fracture			
subjects affected / exposed	0 / 101 (0.00%)	0 / 105 (0.00%)	1 / 99 (1.01%)
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			
Cardiac tamponade			
subjects affected / exposed	1 / 101 (0.99%)	0 / 105 (0.00%)	0 / 99 (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
Myocardial infarction			
subjects affected / exposed	0 / 101 (0.00%)	1 / 105 (0.95%)	0 / 99 (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 ischaemia			
subjects affected / exposed	1 / 101 (0.99%)	0 / 105 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	1 / 101 (0.99%)	0 / 105 (0.00%)	0 / 99 (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
Headache			
subjects affected / exposed	1 / 101 (0.99%)	2 / 105 (1.90%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	2 / 101 (1.98%)	0 / 105 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	1 / 101 (0.99%)	0 / 105 (0.00%)	0 / 99 (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
Myelitis transverse			
subjects affected / exposed	0 / 101 (0.00%)	0 / 105 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 101 (0.99%)	0 / 105 (0.00%)	0 / 99 (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
Eye disorders			
Retinal disorder			

subjects affected / exposed	0 / 101 (0.00%)	0 / 105 (0.00%)	1 / 99 (1.01%)
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			
Abdominal pain			
subjects affected / exposed	0 / 101 (0.00%)	0 / 105 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 101 (0.00%)	1 / 105 (0.95%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 101 (0.99%)	0 / 105 (0.00%)	0 / 99 (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
Vomiting			
subjects affected / exposed	1 / 101 (0.99%)	0 / 105 (0.00%)	0 / 99 (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
Renal and urinary disorders			
Oedematous kidney			
subjects affected / exposed	1 / 101 (0.99%)	0 / 105 (0.00%)	0 / 99 (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
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 101 (0.00%)	0 / 105 (0.00%)	1 / 99 (1.01%)
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	6 / 101 (5.94%)	3 / 105 (2.86%)	3 / 99 (3.03%)
occurrences causally related to treatment / all	0 / 6	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 101 (0.00%)	1 / 105 (0.95%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 101 (0.99%)	0 / 105 (0.00%)	0 / 99 (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
Endocarditis			
subjects affected / exposed	1 / 101 (0.99%)	0 / 105 (0.00%)	0 / 99 (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
Gastroenteritis			
subjects affected / exposed	1 / 101 (0.99%)	0 / 105 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma infection			
subjects affected / exposed	0 / 101 (0.00%)	0 / 105 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 101 (0.00%)	1 / 105 (0.95%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 101 (0.00%)	1 / 105 (0.95%)	2 / 99 (2.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lobar pneumonia			

subjects affected / exposed	1 / 101 (0.99%)	0 / 105 (0.00%)	0 / 99 (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
Meningitis cryptococcal			
subjects affected / exposed	1 / 101 (0.99%)	0 / 105 (0.00%)	0 / 99 (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
Peritonitis			
subjects affected / exposed	0 / 101 (0.00%)	0 / 105 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 101 (1.98%)	2 / 105 (1.90%)	2 / 99 (2.02%)
occurrences causally related to treatment / all	0 / 2	0 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	1 / 101 (0.99%)	0 / 105 (0.00%)	0 / 99 (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
Subcutaneous abscess			
subjects affected / exposed	1 / 101 (0.99%)	0 / 105 (0.00%)	0 / 99 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 101 (0.00%)	0 / 105 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 101 (0.00%)	0 / 105 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo	Anifrolumab 1000 mg	Anifrolumab 300 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 101 (35.64%)	46 / 105 (43.81%)	40 / 99 (40.40%)
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 101 (12.87%)	12 / 105 (11.43%)	12 / 99 (12.12%)
occurrences (all)	21	17	14
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 101 (3.96%)	8 / 105 (7.62%)	4 / 99 (4.04%)
occurrences (all)	4	8	5
Infections and infestations			
Bronchitis			
subjects affected / exposed	4 / 101 (3.96%)	9 / 105 (8.57%)	7 / 99 (7.07%)
occurrences (all)	4	11	7
Nasopharyngitis			
subjects affected / exposed	4 / 101 (3.96%)	12 / 105 (11.43%)	12 / 99 (12.12%)
occurrences (all)	4	20	15
Upper respiratory tract infection			
subjects affected / exposed	10 / 101 (9.90%)	11 / 105 (10.48%)	12 / 99 (12.12%)
occurrences (all)	13	20	14
Urinary tract infection			
subjects affected / exposed	11 / 101 (10.89%)	7 / 105 (6.67%)	15 / 99 (15.15%)
occurrences (all)	18	12	16

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 September 2013	1. Revised text to include the blinding criteria for study site personnel and subjects in Stage I analysis. 2. Corrected the definition of Grade 4 (life threatening) AEs/SAEs to remove reference to disabilities.
09 December 2014	1. Revised the numbering of inclusion and exclusion criteria. 2. Revised exclusion criterion 24 to change the HBV DNA levels to qualify and remain in the study from "undetectable as per central lab" to " \leq 169 copies/mL (29 IU/mL) as per central laboratory". 3. Revised to specify that an unblinded interim analysis is planned for the study. Also added that this analysis will be performed by a limited number of sponsor personnel not involved in the conduct of the study. 4. Revised text to describe the criteria for unblinded staged analyses across Stages I, II, and III. 5. Removed reference to ethylene polyvinyl acetate. 6. Added section header for the followup study and subsequent sections were renumbered. 7. Replaced MedImmune Safety Monitoring Committee with the MedImmune/AstraZeneca safety review committee. 8. Revised section to describe the planned interim analysis. The description for Stage I, II, and III analyses was modified. 9. Removed reference to twosided Type 1 error rate of 0.05 in Sample Size and Power Calculations, Overall Population, and Diagnosticpositive Subpopulation. 10. Increased the sample size of diagnosticpositive subjects per treatment group from 60 to 80.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported