Clinical trial results:
A Multicenter, Randomized, Double-blind, Placebo-controlled, Phase 2 Study Characterizing the Pharmacokinetics, Pharmacodynamics, and Safety of Anifrolumab following subcutaneous administration in Adult Systemic Lupus Erythematosus Subjects with Type I Interferon test high result and active skin manifestations

Summary

EudraCT number	2016-003246-93
Trial protocol	HU PL
Global end of trial date	17 December 2018

Results information

Result version number	v1 (current)
This version publication date	07 September 2019
First version publication date	07 September 2019

Trial information

Trial identification

Sponsor protocol code	D3461C00008

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02962960
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca AB
Sponsor organisation address	One MedImmune Way, Gaithersburg, United States, 20878
Public contact	Global Clinical Lead, AstraZeneca, 1 3013985799, ClinicalTrialTransparency@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca, 1 3013985799, 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	17 December 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 January 2018
Global end of trial reached?	Yes
Global end of trial date	17 December 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To characterize the PK and PD of 150 mg and 300 mg anifrolumab administered as SC injections Q2W as measured by anifrolumab concentrations, PK parameters, 21-gene type I IFN PD signature score and neutralisation ratio at Week 12.

Protection of trial subjects:

The study was conducted in compliance with the Declaration of Helsinki ethical principles and also in compliance with International Conference on Harmonization Good Clinical Practice Guidelines. Local regulatory requirements to protect safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 February 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Hungary: 12
Country: Number of subjects enrolled	Poland: 12
Country: Number of subjects enrolled	Korea, Republic of: 8
Country: Number of subjects enrolled	United States: 4
Worldwide total number of subjects	36
EEA total number of subjects	24

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)	35

From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants type I Interferon (IFN) test-high Systemic Lupus Erythematosus (SLE) subjects with active skin manifestations while receiving Standard of Care (SOC) treatment were eligible for the study.

Pre-assignment

Screening details:

In total, 48 patients were enrolled from 12 participating sites in 4 countries. Twelve patients were enrolled but not randomized due to ineligibility. Of the enrolled patients, 36 patients were randomized, and all received at least one dose of study treatment.

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

Blinding implementation details:

The study was double-blinded with respect to anifrolumab or placebo, but not to dose level (1 or 2 injections). The study was kept blind up until analyses of at Week 12. Randomization was performed via IXRS.

Arms

Are arms mutually exclusive?	Yes
Arm title	Anifrolumab - Lower dose

Arm description:

1ml, once every second week, one subcutaneous injection as added to stand of care, from week 0 to week 50

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

Dosage and administration details:

150mg as added to SOC, given Q2W as one SC injection in a volume of 1mL

Arm title	Anifrolumab - Higher dose

Arm description:

2×1ml, once every second week, two subcutaneous injections as added to stand of care, from week 0 to week 50

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

Dosage and administration details:

300mg as added to SOC, given Q2W as two SC injections in a volume of 1mL each

Arm title	Placebo Comparator

Arm description:

Pooled placebo comparator to both anifrolumab lower and higher doses, adminstered as either 1ml (1 injection) or 2x1ml (2 injections), once every second week, as added to standar of case, from week 0 to

week 50

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

Dosage and administration details:

150 mg (300mg) as added to SOC, given Q2W as one (two) SC injection(s) in a volume of 1mL (each)

Number of subjects in period 1	Anifrolumab - Lower dose	Anifrolumab - Higher dose	Placebo Comparator
Started	14	13	9
Completed	11	11	9
Not completed	3	2	0
Consent withdrawn by subject	1	1	-
Adverse event, non-fatal	1	1	-
Protocol deviation	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Anifrolumab - Lower dose
Reporting group description:	
1ml, once every second week, one subcutaneous injection as added to stand of care, from week 0 to week 50	
Reporting group title	Anifrolumab - Higher dose
Reporting group description:	
2×1ml, once every second week, two subcutaneous injections as added to stand of care, from week 0 to week 50	
Reporting group title	Placebo Comparator
Reporting group description:	
Pooled placebo comparator to both anifrolumab lower and higher doses, adminstered as either 1ml (1 injection) or 2x1ml (2 injections), once every second week, as added to standar of case, from week 0 to week 50	

Reporting group values	Anifrolumab - Lower dose	Anifrolumab - Higher dose	Placebo Comparator
Number of subjects	14	13	9
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	14	13	8
From 65-84 years	0	0	1
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	46.3	41.5	47.8
standard deviation	± 9.1	± 9.2	± 14.2
Sex: Female, Male Units: Subjects			
Female	12	12	8
Male	2	1	1
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	14	13	9
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	6	2	0
Native Hawaiian or Other Pacific Islander	0	0	0

Black or African American	0	0	0
White	8	11	9
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	36		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	35		
From 65-84 years	1		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Subjects			
Female	32		
Male	4		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0		
Not Hispanic or Latino	36		
Unknown or Not Reported	0		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	8		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	28		
More than one race	0		
Unknown or Not Reported	0		

Subject analysis sets	
Subject analysis set title	Placebo Comparator to lower dose
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Placebo comparator to anifrolumab lower dose, adminstered as 1ml (1 injection), once every second week, as added to standard of care, from week 0 to week 50

Subject analysis set title	Placebo Comparator to higher dose

Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Placebo comparator to anifrolumab higher dose, adminstered as 2ml (2 injections), once every second week, as added to standard of care, from week 0 to week 50

Reporting group values	Placebo Comparator to lower dose	Placebo Comparator to higher dose	
Number of subjects	5	4	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	4	4	
From 65-84 years	1	0	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	49.5	46.0	
standard deviation	± 14.5	± 15.8	
Sex: Female, Male Units: Subjects			
Female	5	3	
Male	0	1	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	5	4	
Unknown or Not Reported	0	0	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	5	4	
More than one race	0	0	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Anifrolumab - Lower dose
Reporting group description:	
1ml, once every second week, one subcutaneous injection as added to stand of care, from week 0 to week 50	
Reporting group title	Anifrolumab - Higher dose
Reporting group description:	
2×1ml, once every second week, two subcutaneous injections as added to stand of care, from week 0 to week 50	
Reporting group title	Placebo Comparator
Reporting group description:	
Pooled placebo comparator to both anifrolumab lower and higher doses, adminstered as either 1ml (1 injection) or 2x1ml (2 injections), once every second week, as added to standar of case, from week 0 to week 50	
Subject analysis set title	Placebo Comparator to lower dose
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Placebo comparator to anifrolumab lower dose, adminstered as 1ml (1 injection), once every second week, as added to standard of care, from week 0 to week 50	
Subject analysis set title	Placebo Comparator to higher dose
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Placebo comparator to anifrolumab higher dose, adminstered as 2ml (2 injections), once every second week, as added to standard of care, from week 0 to week 50	

Primary: Maximum concentration of anifrolumab in serum after first dose

End point title	Maximum concentration of anifrolumab in serum after first dose[1]
End point description:	
Maximum concentration (Cmax) of anifrolumab is based on sample collected 5 to 8 days after the first dose of strudy treatment.	
End point type	Primary
End point timeframe:	
Week 0	
Notes:	
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Results are only reported by descriptive statistics, no formal comparisons were performed in this trial.	

End point values	Anifrolumab - Lower dose	Anifrolumab - Higher dose	Placebo Comparator	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	13	0[2]	
Units: mcg/mL				
geometric mean (geometric coefficient of variation)	14.058 (± 49.8151)	28.115 (± 74.4916)	()	

Notes:

[2] - Placebo subjects were not included in PK analyses

Statistical analyses

No statistical analyses for this end point

Primary: Steady-state serum trough (predose) concentration (Ctrough) of Anifrolumab

End point title	Steady-state serum trough (predose) concentration (Ctrough) of Anifrolumab[3]

End point description:

Steady-state serum through concentration (Ctrough) is based on sample collected at Week 12 prior to dosing of study treatment (predose).

End point type	Primary

End point timeframe:

Week 12

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Results are only reported by descriptive statistics, no formal comparisons were performed in this trial.

End point values	Anifrolumab - Lower dose	Anifrolumab - Higher dose	Placebo Comparator	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	11	0[4]	
Units: mcg/mL				
geometric mean (geometric coefficient of variation)	15.618 (± 81.3595)	16.926 (± 9205.6677)	()	

Notes:

[4] - Placebo subjects were not included in PK analyses

Statistical analyses

No statistical analyses for this end point

Primary: 21-gene type 1 IFN signature score (fold-change)

End point title	21-gene type 1 IFN signature score (fold-change)[5]

End point description:

21-gene type I IFN signature score (fold change) is based on samples collected both at baseline and Week 12 prior to dosing of study treatment. Levels of 21-gene type I IFN pharmacodynamics signature is derived as relative to a pooled normal control.

End point type	Primary

End point timeframe:

Week 12

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Results are only reported by descriptive statistics, no formal comparisons were performed in this trial.

End point values	Anifrolumab - Lower dose	Anifrolumab - Higher dose	Placebo Comparator	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	11	9	
Units: fold change				
arithmetic mean (standard deviation)	3.2 (± 3.69)	3.5 (± 5.73)	14.3 (± 6.68)	

Statistical analyses

No statistical analyses for this end point

Primary: 21-gene type 1 IFN neutralization ratio (percent suppression of fold change)

End point title	21-gene type 1 IFN neutralization ratio (percent suppression of fold change)[6]

End point description:

21-gene type I IFN signature score (fold change) is based on samples collected both at baseline and Week 12 prior to dosing of study treatment. Levels of 21-gene type I IFN pharmacodynamics signature is derived as relative to a pooled normal control, as the median of 100-(((baseline-Week 12)/baseline)*100) for the 21 genes.

End point type	Primary

End point timeframe:

Week 12

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Results are only reported by descriptive statistics, no formal comparisons were performed in this trial.

End point values	Anifrolumab - Lower dose	Anifrolumab - Higher dose	Placebo Comparator	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	11	9	
Units: % neutralization				
arithmetic mean (standard deviation)	77.5 (± 24.16)	80.5 (± 36.65)	15.1 (± 49.63)	

Statistical analyses

No statistical analyses for this end point

Secondary: Antidrug antibody (ADA)

End point title	Antidrug antibody (ADA)

End point description:

Post-baseline ADA incidence.

End point type	Secondary

End point timeframe:

Baseline to Week 52

End point values	Anifrolumab - Lower dose	Anifrolumab - Higher dose	Placebo Comparator	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	13	9	
Units: Subject	1	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Neutralizing antibodies (nAb)

End point title	Neutralizing antibodies (nAb)

End point description:

Incidence of detectable nAb in post-baseline ADA positive participants.

End point type	Secondary

End point timeframe:

Baseline to Week 52

End point values	Anifrolumab - Lower dose	Anifrolumab - Higher dose	Placebo Comparator	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	1	0[7]	
Units: Subject	0	0		

Notes:

[7] - Only ADA positive subjects are included in this analysis

Statistical analyses

No statistical analyses for this end point

Secondary: Number AEs (Adverse events) and SAEs (serious adverse events), including adverse events of special interest (AESI)

End point title	Number AEs (Adverse events) and SAEs (serious adverse events), including adverse events of special interest (AESI)

End point description:

Number of participants with any AEs (Adverse events), any SAEs (serious adverse events), and any adverse events of special interest (AESI) are summarized. More details are reported in the Adverse Events section.

End point type	Secondary

End point timeframe:

Baseline to Week 60

End point values	Anifrolumab - Lower dose	Anifrolumab - Higher dose	Placebo Comparator	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	13	9	
Units: Subject				
Any adverse event	12	11	7	
Any serious adverse event	4	2	0	
Any adverse event of special interest	5	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline for vital signs

End point title	Change from baseline for vital signs[8]

End point description:

Change from baseline for vital signs.

End point type	Secondary

End point timeframe:

Baseline to Week 60

Notes:

[8] - 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: Results are only reported by descriptive statistics, no formal comparisons were performed in this trial.

End point values	Anifrolumab - Lower dose	Anifrolumab - Higher dose	Placebo Comparator to lower dose	Placebo Comparator to higher dose
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	14	13	5	4
Units: mmHg				
arithmetic mean (standard deviation)				
Systolic Blood Pressure (mmHg) - Week 12	-4.1 (± 12.08)	3 (± 6.63)	-5.8 (± 13.99)	7.3 (± 8.96)
Systolic Blood Pressure (mmHg) - Week 52	2.1 (± 10.96)	-1.7 (± 12.96)	3.4 (± 8.53)	12.5 (± 19.36)
Systolic Blood Pressure (mmHg) - Week 60	4.1 (± 19.70)	-2.8 (± 14.91)	12.2 (± 8.61)	4.5 (± 7.14)
Diastolic Blood Pressure (mmHg) - Week 12	-2.0 (± 10.02)	2.4 (± 6.71)	-3.8 (± 6.50)	4.3 (± 4.35)
Diastolic Blood Pressure (mmHg) - Week 52	0.1 (± 6.87)	2.9 (± 7.54)	-0.4 (± 7.13)	6.8 (± 5.38)
Diastolic Blood Pressure (mmHg) - Week 60	3.6 (± 12.23)	-0.8 (± 6.86)	-1.0 (± 8.22)	8.8 (± 6.29)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline for physical examination

End point title	Change from baseline for physical examination[9]

End point description:

Physical examination is reported as change from baseline in body weight.

End point type	Secondary

End point timeframe:

Baseline to Week 60

Notes:

[9] - 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: Results are only reported by descriptive statistics, no formal comparisons were performed in this trial.

End point values	Anifrolumab - Lower dose	Anifrolumab - Higher dose	Placebo Comparator to lower dose	Placebo Comparator to higher dose
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	14	13	5	4
Units: kilograms				
arithmetic mean (standard deviation)				
Week 12	-1.81 (± 2.674)	1.37 (± 3.113)	0.7 (± 1.889)	0.98 (± 2.904)
Week 52	-2.83 (± 4.683)	2.52 (± 6.495)	0.30 (± 3.338)	3.90 (± 5.608)
Week 60	-1.81 (± 3.858)	2.93 (± 6.463)	1.06 (± 4.020)	3.60 (± 5.300)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline for 12-lead ECG

End point title	Change from baseline for 12-lead ECG[10]

End point description:

The 12-lead ECG measurements were assessed by the investigators, and reported as normal, abnormal (not clinically significant [NCS]), abnormal (clinically significant [CS]), or not done. No occurrence of abnormal (CS) was observed.

End point type	Secondary

End point timeframe:

Baseline to Week 52

Notes:

[10] - 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: Results are only reported by descriptive statistics, no formal comparisons were performed in this trial.

End point values	Anifrolumab - Lower dose	Anifrolumab - Higher dose	Placebo Comparator to lower dose	Placebo Comparator to higher dose
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	14	13	5	4
Units: Subject				
Normal at baseline - Normal at Week 52	7	10	5	3
Normal at baseline - Abnormal (NCS) at Week 52	1	1	0	0
Normal at baseline - not done at Week 52	1	2	0	0
Abnormal (NCS) at baseline - Normal at Week 52	2	0	0	1
Abnormal (NCS) baseline - Abnormal (NCS) Week 52	1	0	0	0
Abnormal (NCS) at baseline - not done at Week 52	2	0	0	0
Not done at baseline - Normal at Week 52	0	0	0	0
Not done at baseline - Abnormal (NCS) at Week 52	0	0	0	0
Not done at baseline - Not done at Week 52	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Value of Haematology blood tests to detect change from baseline

End point title	Value of Haematology blood tests to detect change from baseline[11]

End point description:

Change from baseline in haematology blood tests (haemoglobin, leucocytes [particle concentration], platelets [particle concentration]) are reported.

End point type	Secondary

End point timeframe:

Baseline to Week 60

Notes:

[11] - 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: Results are only reported by descriptive statistics, no formal comparisons were performed in this trial.

End point values	Anifrolumab - Lower dose	Anifrolumab - Higher dose	Placebo Comparator to lower dose	Placebo Comparator to higher dose
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	14	13	5	4
Units: According to blood test measure				
arithmetic mean (standard deviation)				
Haemoglobin (g/L) - Week 12	-0.2 (± 9.07)	0.7 (± 7.4)	-0.5 (± 7.14)	4.8 (± 5.91)
Haemoglobin (g/L) - Week 52	-1.1 (± 13.92)	0.1 (± 11.65)	-4.8 (± 3.83)	7 (± 5.94)
Haemoglobin (g/L) - Week 60	0.8 (± 12.97)	0 (± 10.43)	-5.4 (± 5.68)	5.8 (± 6.85)

Leucocytes (10^9/L) - Week 12	0.491 (± 1.5806)	3.165 (± 2.2706)	0.867 (± 1.0999)	1.96 (± 1.9487)
Leucocytes (10^9/L) - Week 52	1.041 (± 1.5794)	2.457 (± 2.3891)	0.236 (± 1.0107)	0.080 (± 1.4798)
Leucocytes (10^9/L) - Week 60	-0.012 (± 1.5489)	1.474 (± 1.6490)	0.776 (± 2.1779)	1.23 (± 1.6687)
Platelets (10^9/L) - Week 12	7.8 (± 65.28)	45.2 (± 67.41)	10.3 (± 24.54)	17.0 (± 42.58)
Platelets (10^9/L) - Week 52	28.0 (± 74.28)	46.1 (± 74.91)	6.6 (± 64.24)	-2.0 (± 33.85)
Platelets (10^9/L) - Week 60	-19.1 (± 53.48)	39.0 (± 60.33)	24.4 (± 65.73)	-2.8 (± 28.43)

Statistical analyses

No statistical analyses for this end point

Secondary: Value of Urinalysis tests to detect change from baseline

End point title	Value of Urinalysis tests to detect change from baseline[12]

End point description:

Change from baseline in urinalysis (total protein and protein-creatinine ratio) are reported.

End point type	Secondary

End point timeframe:

Baseline to Week 60

Notes:

[12] - 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: Results are only reported by descriptive statistics, no formal comparisons were performed in this trial.

End point values	Anifrolumab - Lower dose	Anifrolumab - Higher dose	Placebo Comparator to lower dose	Placebo Comparator to higher dose
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	14	13	5	4
Units: According to urinalysis measure				
arithmetic mean (standard deviation)				
Protein, Total (g/L) - Week 12	0.7669 (± 2.71221)	-0.0744 (± 0.76445)	0 (± 0)	0.3443 (± 0.34301)
Protein, Total (g/L) - Week 52	-0.0029 (± 0.08124)	-0.0011 (± 0.33468)	0 (± 0)	0.1143 (± 0.24476)
Protein, Total (g/L) - Week 60	0.1151 (± 0.12514)	-0.1790 (± 0.83066)	0.003 (± 0.00671)	0.3975 (± 0.82602)
Protein/Creatinine (g/g) - Week 12	1.37029 (± 5.186672)	-0.13007 (± 1.123807)	-0.03056 (± 0.056701)	0.32764 (± 0.337631)
Protein/Creatinine (g/g) - Week 52	0.03756 (± 0.135157)	-0.00465 (± 0.183327)	-0.00781 (± 0.047671)	0.080930 (± 1.581772)
Protein/Creatinine (g/g) - Week 60	0.02578 (± 0.119862)	-0.28836 (± 1.185347)	-0.03501 (± 0.061888)	0.46178 (± 0.899886)

Statistical analyses

No statistical analyses for this end point

Secondary: Value of Clinical Chemistry blood tests to detect change from baseline (serum)

End point title	Value of Clinical Chemistry blood tests to detect change from baseline (serum)[13]

End point description:

Change from baseline in clinical chemistry blood tests (Alanine Aminotransferase, Aspartate Aminotransferase, Creatinine) are reported.

End point type	Secondary

End point timeframe:

Baseline to Week 60

Notes:

[13] - 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: Results are only reported by descriptive statistics, no formal comparisons were performed in this trial.

End point values	Anifrolumab - Lower dose	Anifrolumab - Higher dose	Placebo Comparator to lower dose	Placebo Comparator to higher dose
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	14	13	5	4
Units: According to urinalysis measure				
arithmetic mean (standard deviation)				
Alanine Aminotransferase (ukat/L) - Week 12	0.00769 (± 0.147479)	-0.13003 (± 0.431764)	-0.05418 (± 0.045905)	0.02501 (± 0.134397)
Alanine Aminotransferase (ukat/L) - Week 52	-0.06335 (± 0.119642)	-0.05607 (± 0.556152)	-0.06335 (± 0.047735)	0.04167 (± 0.169182)
Alanine Aminotransferase (ukat/L) - Week 60	-0.01297 (± 0.043131)	0.09446 (± 0.365981)	-0.04334 (± 0.032495)	-0.01667 (± 0.18127)
Aspartate Aminotransferase (ukat/L) - Week 12	-0.01154 (± 0.065765)	-0.10502 (± 0.169099)	0.00417 (± 0.059911)	0.03334 (± 0.105430)
Aspartate Aminotransferase (ukat/L) - Week 52	-0.04834 (± 0.066424)	-0.05304 (± 0.196369)	0.00333 (± 0.090847)	0.09169 (± 0.100482)
Aspartate Aminotransferase (ukat/L) - Week 60	-0.01111 (± 0.058937)	0.04816 (± 0.123752)	0 (± 0.050010)	-0.02501 (± 0.099555)
Creatinine (umol/L) - Week 12	4.385 (± 8.5799)	-3.6 (± 11.2467)	5.5 (± 6.3509)	5.25 (± 9.8446)
Creatinine (umol/L) - Week 52	12.2 (± 33.2597)	-7.273 (± 19.5862)	0.2 (± 13.9714)	2.5 (± 5.5076)
Creatinine (umol/L) - Week 60	7.316 (± 8.7449)	-5.556 (± 12.8463)	5.0 (± 10.4163)	6.5 (± 12.5033)

Statistical analyses

No statistical analyses for this end point

Secondary: Value of Inflammatory marker panel blood tests to detect change from baseline

End point title	Value of Inflammatory marker panel blood tests to detect change from baseline

End point description:

Change from baseline in the Erythrocyte Sedimentation Rate (ESR) inflammatory marker is reported.

End point type	Secondary
End point timeframe: Baseline to Week 60	

End point values	Anifrolumab - Lower dose	Anifrolumab - Higher dose	Placebo Comparator	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	13	9	
Units: mm				
arithmetic mean (standard deviation)				
ESR - Week 12	-3.0 (± 20.37)	-7.2 (± 15.46)	-11.9 (± 15.36)	
ESR - Week 52	5.6 (± 25.58)	-6.7 (± 12.25)	-16.0 (± 10.95)	
ESR - Week 60	14.6 (± 38.77)	-1.0 (± 21.84)	2.2 (± 22.48)	

Statistical analyses

No statistical analyses for this end point

Secondary: Value of Autoantibody blood panel blood tests to detect change from baseline

End point title	Value of Autoantibody blood panel blood tests to detect change from baseline[14]
End point description: Change from baseline in Anti-Double Stranded DNA IgG (anti-dsDNA) is reported.	
End point type	Secondary
End point timeframe: Baseline to Week 60	

Notes:

[14] - 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: Results are only reported by descriptive statistics, no formal comparisons were performed in this trial.

End point values	Anifrolumab - Lower dose	Anifrolumab - Higher dose	Placebo Comparator to lower dose	Placebo Comparator to higher dose
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	9	8	3	3
Units: IU/mL				
arithmetic mean (standard deviation)				
anti-dsDNA - Week 12	-42.09 (± 256.228)	-84.97 (± 231.489)	-37.0 (± 19.799)	-97.33 (± 151.596)
anti-dsDNA - Week 52	-99.04 (± 288.183)	8.70 (± 27.308)	-13.0 (± 50.229)	-76.87 (± 127.433)
anti-dsDNA - Week 60	52.67 (± 144.220)	16.53 (± 30.528)	-21.33 (± 54.921)	-76.73 (± 141.525)

Statistical analyses

No statistical analyses for this end point

Secondary: Value of Infection-related blood tests to detect change from baseline

End point title	Value of Infection-related blood tests to detect change from baseline[15]

End point description:

Change from screening in Hepatitis B core antibody was monitored during the study for participants tested positive at screening.

End point type	Secondary

End point timeframe:

Baseline to Week 60

Notes:

[15] - 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: Results are only reported by descriptive statistics, no formal comparisons were performed in this trial.

End point values	Anifrolumab - Lower dose	Anifrolumab - Higher dose	Placebo Comparator to lower dose	Placebo Comparator to higher dose
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	0[16]	0[17]	0[18]	0[19]
Units: Subject				
Positive post-baseline				

Notes:

[16] - No subjects with Hepatitis B core antibody positive at screening

[17] - No subjects with Hepatitis B core antibody positive at screening

[18] - No subjects with Hepatitis B core antibody positive at screening

[19] - No subjects with Hepatitis B core antibody positive at screening

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

52 weeks

Adverse event reporting additional description:

An unfavorable change in the health of a participant, including abnormal laboratory findings, that happens during the clinical study (from and including the day of first dose of investigational product, up to, and including, the date of last dose of IMP plus 14 days). This change may or may not be caused by the treatment being studied.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Anifrolumab - Lower dose

Reporting group description:

1ml, once every second week, one subcutaneous injection as added to stand of care, from week 0 to week 50

Reporting group title	Placebo Comparator

Reporting group description:

Pooled placebo comparator to both anifrolumab lower and higher doses, adminstered as either 1ml (1 injection) or 2x1ml (2 injections), once every second week, as added to standar of case, from week 0 to week 50

Reporting group title	Anifrolumab - Higher dose

Reporting group description:

2×1ml, once every second week, two subcutaneous injections as added to stand of care, from week 0 to week 50

Serious adverse events	Anifrolumab - Lower dose	Placebo Comparator	Anifrolumab - Higher dose
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 14 (28.57%)	0 / 9 (0.00%)	2 / 13 (15.38%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Nervous system disorders			
Transient Ischaemic Attack			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Mouth Ulceration			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (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

Renal and urinary disorders			
Lupus Nephritis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 1	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	1 / 14 (7.14%)	0 / 9 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Herpes Zoster			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (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
Otitis Media Acute			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (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

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

Non-serious adverse events	Anifrolumab - Lower dose	Placebo Comparator	Anifrolumab - Higher dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 14 (85.71%)	7 / 9 (77.78%)	11 / 13 (84.62%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 14 (0.00%)	1 / 9 (11.11%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Pregnancy, puerperium and perinatal conditions			
Anembryonic Gestation			
subjects affected / exposed	0 / 14 (0.00%)	1 / 9 (11.11%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			

Chest Pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 9 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Face Oedema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 9 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	2
Feeling Hot			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Oedema Peripheral			
subjects affected / exposed	0 / 14 (0.00%)	0 / 9 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 9 (11.11%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 14 (0.00%)	0 / 9 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	2
Reproductive system and breast disorders			
Endometrial Hyperplasia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Nasal Inflammation			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0

Nasal Septum Perforation			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Pleural Effusion			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Productive Cough			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Panic Attack			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Investigations			
Mycobacterium Tuberculosis Complex Test Positive			
subjects affected / exposed	0 / 14 (0.00%)	0 / 9 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Foot Fracture			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Spinal Compression Fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 9 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Subcutaneous Haematoma			
subjects affected / exposed	0 / 14 (0.00%)	0 / 9 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Cardiac disorders			
Atrial Fibrillation			

subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Palpitations			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Pericardial Cyst			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	2 / 14 (14.29%)	0 / 9 (0.00%)	2 / 13 (15.38%)
occurrences (all)	2	0	2
Hypoaesthesia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Migraine			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	0 / 14 (0.00%)	0 / 9 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Syncope			
subjects affected / exposed	0 / 14 (0.00%)	1 / 9 (11.11%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 9 (11.11%)	0 / 13 (0.00%)
occurrences (all)	1	1	0
Eye disorders			
Chalazion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 9 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Myopia			

subjects affected / exposed	0 / 14 (0.00%)	1 / 9 (11.11%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Uveitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Abdominal Pain			
subjects affected / exposed	1 / 14 (7.14%)	1 / 9 (11.11%)	0 / 13 (0.00%)
occurrences (all)	1	1	0
Dental Caries			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	2 / 14 (14.29%)	2 / 9 (22.22%)	0 / 13 (0.00%)
occurrences (all)	2	2	0
Food Poisoning			
subjects affected / exposed	0 / 14 (0.00%)	0 / 9 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Gastrooesophageal Reflux Disease			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Haemorrhoids			
subjects affected / exposed	0 / 14 (0.00%)	0 / 9 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Mouth Ulceration			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Paraesthesia Oral			
subjects affected / exposed	0 / 14 (0.00%)	0 / 9 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1

Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Miliaria			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Urticaria			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Proteinuria			
subjects affected / exposed	0 / 14 (0.00%)	1 / 9 (11.11%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Renal Impairment			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	2 / 14 (14.29%)	1 / 9 (11.11%)	1 / 13 (7.69%)
occurrences (all)	2	1	1
Osteoporosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 9 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Spinal Pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Abscess Limb			
subjects affected / exposed	0 / 14 (0.00%)	1 / 9 (11.11%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Acute Sinusitis			

subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	1 / 14 (7.14%)	1 / 9 (11.11%)	3 / 13 (23.08%)
occurrences (all)	1	1	5
Conjunctivitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 9 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Conjunctivitis Viral			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Herpes Zoster			
subjects affected / exposed	2 / 14 (14.29%)	1 / 9 (11.11%)	0 / 13 (0.00%)
occurrences (all)	2	1	0
Influenza			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Labyrinthitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 9 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Laryngitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	3 / 14 (21.43%)	1 / 9 (11.11%)	2 / 13 (15.38%)
occurrences (all)	3	1	2
Pharyngitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 9 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	2
Sinusitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 9 (11.11%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Upper Respiratory Tract Infection			
subjects affected / exposed	5 / 14 (35.71%)	3 / 9 (33.33%)	1 / 13 (7.69%)
occurrences (all)	9	3	1
Urinary Tract Infection			

subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	0 / 9 (0.00%) 0	1 / 13 (7.69%) 1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported