



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, administered 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: 2x1ml, 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, administered 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, administered 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, administered 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: 2x1ml, 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, administered 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, administered 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, administered 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 (\pm 49.8151) | 28.115 (\pm 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 (C_{trough}) of Anifrolumab

| | |
|-----------------|--|
| End point title | Steady-state serum trough (predose) concentration (C _{trough}) of Anifrolumab ^[3] |
|-----------------|--|

End point description:

Steady-state serum trough concentration (C_{trough}) 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 $100 - (((\text{baseline} - \text{Week 12}) / \text{baseline}) * 100)$ 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

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 (\pm 0.147479) | -0.13003 (\pm 0.431764) | -0.05418 (\pm 0.045905) | 0.02501 (\pm 0.134397) |
| Alanine Aminotransferase (ukat/L) - Week 52 | -0.06335 (\pm 0.119642) | -0.05607 (\pm 0.556152) | -0.06335 (\pm 0.047735) | 0.04167 (\pm 0.169182) |
| Alanine Aminotransferase (ukat/L) - Week 60 | -0.01297 (\pm 0.043131) | 0.09446 (\pm 0.365981) | -0.04334 (\pm 0.032495) | -0.01667 (\pm 0.18127) |
| Aspartate Aminotransferase (ukat/L) - Week 12 | -0.01154 (\pm 0.065765) | -0.10502 (\pm 0.169099) | 0.00417 (\pm 0.059911) | 0.03334 (\pm 0.105430) |
| Aspartate Aminotransferase (ukat/L) - Week 52 | -0.04834 (\pm 0.066424) | -0.05304 (\pm 0.196369) | 0.00333 (\pm 0.090847) | 0.09169 (\pm 0.100482) |
| Aspartate Aminotransferase (ukat/L) - Week 60 | -0.01111 (\pm 0.058937) | 0.04816 (\pm 0.123752) | 0 (\pm 0.050010) | -0.02501 (\pm 0.099555) |
| Creatinine (umol/L) - Week 12 | 4.385 (\pm 8.5799) | -3.6 (\pm 11.2467) | 5.5 (\pm 6.3509) | 5.25 (\pm 9.8446) |
| Creatinine (umol/L) - Week 52 | 12.2 (\pm 33.2597) | -7.273 (\pm 19.5862) | 0.2 (\pm 13.9714) | 2.5 (\pm 5.5076) |
| Creatinine (umol/L) - Week 60 | 7.316 (\pm 8.7449) | -5.556 (\pm 12.8463) | 5.0 (\pm 10.4163) | 6.5 (\pm 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, administered 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:

2x1ml, 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 occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 14 (7.14%) 0 / 1 0 / 0 | 0 / 9 (0.00%) 0 / 0 0 / 0 | 1 / 13 (7.69%) 0 / 1 0 / 0 |
| Musculoskeletal and connective tissue disorders Systemic Lupus Erythematosus subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 14 (7.14%) 0 / 1 0 / 0 | 0 / 9 (0.00%) 0 / 0 0 / 0 | 1 / 13 (7.69%) 0 / 1 0 / 0 |
| Infections and infestations Herpes Zoster subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 14 (7.14%) 1 / 1 0 / 0 | 0 / 9 (0.00%) 0 / 0 0 / 0 | 0 / 13 (0.00%) 0 / 0 0 / 0 |
| Otitis Media Acute subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 14 (7.14%) 1 / 1 0 / 0 | 0 / 9 (0.00%) 0 / 0 0 / 0 | 0 / 13 (0.00%) 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 occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 9 (11.11%) 1 | 0 / 13 (0.00%) 0 |
| Pregnancy, puerperium and perinatal conditions Anembryonic Gestation subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 9 (11.11%) 1 | 0 / 13 (0.00%) 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 occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 9 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Pleural Effusion subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 9 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Productive Cough subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 9 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Rhinorrhoea subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 9 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 2 | 0 / 9 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Panic Attack subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 9 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Investigations Mycobacterium Tuberculosis Complex Test Positive subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 13 (7.69%) 1 |
| Injury, poisoning and procedural complications Foot Fracture subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 9 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Spinal Compression Fracture subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 13 (7.69%) 1 |
| Subcutaneous Haematoma subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 13 (7.69%) 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 | 1 / 14 (7.14%) | 0 / 9 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 1 | 0 | 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