



## Clinical trial results:

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

#### Summary

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

#### Results information

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

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | D3461C00005 |
|-----------------------|-------------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |                                                                                                  |
|------------------------------|--------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | AstraZeneca AB                                                                                   |
| Sponsor organisation address | Forskargatan 18, Sudertalje, Sweden, 151 85                                                      |
| Public contact               | Global Clinical Leader, AstraZeneca AB, +46 317761000, ClinicalTrialTransparency@astrazeneca.com |
| Scientific contact           | Global Clinical Leader, AstraZeneca AB, +46 317761000, ClinicalTrialTransparency@astrazeneca.com |

Notes:

#### Paediatric regulatory details

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

Notes:

## Results analysis stage

|                                                      |                |
|------------------------------------------------------|----------------|
| Analysis stage                                       | Final          |
| Date of interim/final analysis                       | 23 August 2018 |
| Is this the analysis of the primary completion data? | Yes            |
| Primary completion date                              | 23 August 2018 |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 23 August 2018 |
| Was the trial ended prematurely?                     | No             |

Notes:

## General information about the trial

Main objective of the trial:

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

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

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

Notes:

## Population of trial subjects

### Subjects enrolled per country

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

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

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|-------------------------------------------|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 0   |
| Adults (18-64 years)                      | 437 |
| From 65 to 84 years                       | 20  |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

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

### Pre-assignment

Screening details:

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

### Period 1

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

### Arms

|                              |                    |
|------------------------------|--------------------|
| Are arms mutually exclusive? | Yes                |
| <b>Arm title</b>             | Anifrolumab 150 mg |

Arm description:

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

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

Dosage and administration details:

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

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | Anifrolumab 300 mg |
|------------------|--------------------|

Arm description:

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

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

Dosage and administration details:

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

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Placebo |
|------------------|---------|

Arm description:

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

|          |         |
|----------|---------|
| Arm type | Placebo |
|----------|---------|

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

Dosage and administration details:

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

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

## Baseline characteristics

### Reporting groups

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

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

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

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





## End points

### End points reporting groups

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

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

|                            |                                       |
|----------------------------|---------------------------------------|
| Subject analysis set title | Placebo Baseline OCS $\geq 10$ mg/day |
| Subject analysis set type  | Full analysis                         |

Subject analysis set description:

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

|                            |                                                   |
|----------------------------|---------------------------------------------------|
| Subject analysis set title | Anifrolumab 150 mg CLASI Activity Score $\geq 10$ |
| Subject analysis set type  | Full analysis                                     |

Subject analysis set description:

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

|                            |                                                   |
|----------------------------|---------------------------------------------------|
| Subject analysis set title | Anifrolumab 300 mg CLASI Activity Score $\geq 10$ |
| Subject analysis set type  | Full analysis                                     |

Subject analysis set description:

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

|                            |                                        |
|----------------------------|----------------------------------------|
| Subject analysis set title | Placebo CLASI Activity Score $\geq 10$ |
| Subject analysis set type  | Full analysis                          |

Subject analysis set description:

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

---

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

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

End point description:

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

Reduction from baseline of  $\geq 4$  points in the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K)

No new organ systems affected, defined by 1 or more British Isles Lupus Assessment Group (BILAG-2004) A or 2 or more BILAG-2004 B items

No worsening from baseline in participants lupus disease activity. Worsening was defined as an increase of  $\geq 0.30$  points on a 3-point Physician's Global Assessment (PGA) visual analogue scale (VAS)

No discontinuation of investigational product and no use of restricted medications beyond the pre-specified analysis threshold.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Week 52

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

## Statistical analyses

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

Notes:

[1] - Nominal p-value

|                                                                                                                                                                                                                                                                                                                                                                                                 |                                  |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                                                                                                                                                               | Analysis of Treatment Difference |
| Statistical analysis description:                                                                                                                                                                                                                                                                                                                                                               |                                  |
| The difference in estimates and associated 95% CI are weighted and are calculated using a stratified Cochran-Mantel-Haenszel (CMH) approach, with stratification factors (SLEDAI-2K score at screening [ $<10$ points vs $\geq 10$ points], Week 0 OCS dose [ $<10$ mg/day vs $\geq 10$ mg/day prednisone or equivalent] and type I IFN gene signature test result at screening [high vs low]). |                                  |
| Comparison groups                                                                                                                                                                                                                                                                                                                                                                               | Anifrolumab 150 mg v Placebo     |
| Number of subjects included in analysis                                                                                                                                                                                                                                                                                                                                                         | 277                              |
| Analysis specification                                                                                                                                                                                                                                                                                                                                                                          | Pre-specified                    |
| Analysis type                                                                                                                                                                                                                                                                                                                                                                                   | superiority                      |
| Parameter estimate                                                                                                                                                                                                                                                                                                                                                                              | Difference in proportions        |
| Point estimate                                                                                                                                                                                                                                                                                                                                                                                  | -2.6                             |
| Confidence interval                                                                                                                                                                                                                                                                                                                                                                             |                                  |
| level                                                                                                                                                                                                                                                                                                                                                                                           | 95 %                             |
| sides                                                                                                                                                                                                                                                                                                                                                                                           | 2-sided                          |
| lower limit                                                                                                                                                                                                                                                                                                                                                                                     | -14.7                            |
| upper limit                                                                                                                                                                                                                                                                                                                                                                                     | 9.6                              |

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

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

End point description:

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

Reduction from baseline of  $\geq 4$  points in the SLEDAI-2K

No new organ systems affected, defined by 1 or more BILAG-2004) A or 2 or more BILAG-2004 B

No worsening from baseline in participants lupus disease activity. Worsening was defined as an increase of  $\geq 0.30$  points on a 3-point PGA VAS

No discontinuation of investigational product and no use of restricted medications beyond the pre-specified analysis threshold.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Week 52              |           |

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

### Statistical analyses

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

Notes:

[2] - Nominal p-value

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

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

End point description:

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

Achieve an OCS dose of  $\leq 7.5$  mg/day prednisone or equivalent by Week 40

Maintain an OCS dose  $\leq 7.5$  mg/day prednisone or equivalent from Week 40 to Week 52

No discontinuation of investigational product and no use of restricted medications beyond the pre-specified analysis threshold.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Week 52              |           |

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

## Statistical analyses

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

Notes:

[3] - Nominal p-value

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

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

End point description:

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

Achieve ≥50% reduction of CLASI activity score at Week 12 compared to baseline

No discontinuation of investigational product and no use of restricted medications beyond the pre-specified analysis threshold before assessment.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 12

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

## Statistical analyses

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

Notes:

[4] - Nominal p-value

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

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

End point description:

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

Reduction from baseline of ≥4 points in the SLEDAI-2K

No new organ systems affected as defined by 1 or more BILAG-2004 A or 2 or more BILAG-2004 B items

No worsening from baseline in participants lupus disease activity. Worsening was defined as an increase of ≥0.30 points on a 3-point PGA VAS

No discontinuation of investigational product and no use of restricted medications beyond the pre-specified threshold.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 24

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

## Statistical analyses

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

Notes:

[5] - Nominal p-value

## Secondary: Annualized Flare Rate

|                 |                       |
|-----------------|-----------------------|
| End point title | Annualized Flare Rate |
|-----------------|-----------------------|

End point description:

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

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 52

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

## Statistical analyses

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                  |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Analysis of Treatment Difference |
| Statistical analysis description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                  |
| Analysed using a negative binomial regression model. The response variable in the model is the number of flares over the 52-week treatment period. The model includes covariates of treatment group, and the stratification factors (SLEDAI-2K score at screening [ $<10$ points vs $\geq 10$ points], Week 0 OCS dose [ $<10$ mg/day vs $\geq 10$ mg/day prednisone or equivalent] and type I IFN gene signature test result at screening [high vs low]). The logarithm of the follow-up time is used as an offset variable |                                  |
| Comparison groups                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Anifrolumab 300 mg v Placebo     |
| Number of subjects included in analysis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 364                              |
| Analysis specification                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Pre-specified                    |
| Analysis type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                  |
| P-value                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | = 0.258 <sup>[6]</sup>           |
| Method                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Cochran-Mantel-Haenszel          |
| Parameter estimate                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Rate Ratio                       |
| Point estimate                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 0.83                             |
| Confidence interval                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                  |
| level                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 95 %                             |
| sides                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 2-sided                          |
| lower limit                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 0.6                              |
| upper limit                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 1.14                             |

Notes:

[6] - Nominal p-value

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

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

End point description:

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

All criteria related to SRI(4) (please see primary endpoint) plus:

Reduction of all baseline BILAG-2004 A to B/C/D and baseline BILAG-2004 B to C/D, and no BILAG-2004 worsening in other organ systems, as defined by 1 or more BILAG-2004 A or 1 or more new BILAG-2004 B item

No discontinuation of investigational product and no use of restricted medications beyond the revised post-hoc analysis threshold before assessment.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 52



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

## Statistical analyses

| Statistical analysis title                                                                                                                                                                                                                                                                                                                                                     | Analysis of Treatment Difference |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|
| Statistical analysis description:                                                                                                                                                                                                                                                                                                                                              |                                  |
| The difference in estimates and associated 95% CI are weighted and are calculated using a stratified Cochran-Mantel-Haenszel (CMH) approach, with stratification factors (SLEDAI-2K score at screening [<10 points vs ≥ 10 points], Week 0 OCS dose [<10 mg/day vs ≥10 mg/day prednisone or equivalent] and type I IFN gene signature test result at screening [high vs low]). |                                  |
| Comparison groups                                                                                                                                                                                                                                                                                                                                                              | Anifrolumab 300 mg v Placebo     |
| Number of subjects included in analysis                                                                                                                                                                                                                                                                                                                                        | 364                              |
| Analysis specification                                                                                                                                                                                                                                                                                                                                                         | Pre-specified                    |
| Analysis type                                                                                                                                                                                                                                                                                                                                                                  |                                  |
| Parameter estimate                                                                                                                                                                                                                                                                                                                                                             | Difference in proportions        |
| Point estimate                                                                                                                                                                                                                                                                                                                                                                 | 10.1                             |
| Confidence interval                                                                                                                                                                                                                                                                                                                                                            |                                  |
| level                                                                                                                                                                                                                                                                                                                                                                          | 95 %                             |
| sides                                                                                                                                                                                                                                                                                                                                                                          | 2-sided                          |
| lower limit                                                                                                                                                                                                                                                                                                                                                                    | 0.6                              |
| upper limit                                                                                                                                                                                                                                                                                                                                                                    | 19.7                             |

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

| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Number of Participants Reporting One or More Adverse Events (AEs) |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                   |
| An AE is defined as any untoward medical occurrence in a clinical investigation participant administered a drug; it does not necessarily have to have a causal relationship with this treatment. AEs were collected throughout the duration of the study, from baseline until end of follow-up (a maximum of 12 weeks post last dose [Week 48]), or until Week 52 for participants who enrolled onto the long term extension (LTE). The reported value is inclusive of serious and non-serious AEs. |                                                                   |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Secondary                                                         |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                   |
| Baseline to End of Trial (Maximum of 60 weeks)                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                   |

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

## Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to End of Trial (Maximum of 60 weeks)

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

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with Markedly Abnormal Vital Signs

|                 |                                                           |
|-----------------|-----------------------------------------------------------|
| End point title | Number of Participants with Markedly Abnormal Vital Signs |
|-----------------|-----------------------------------------------------------|

End point description:

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

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to End of Trial (Maximum of 60 weeks)

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

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with Markedly Abnormal Physical Examinations

|                 |                                                                     |
|-----------------|---------------------------------------------------------------------|
| End point title | Number of Participants with Markedly Abnormal Physical Examinations |
|-----------------|---------------------------------------------------------------------|

End point description:

Physical examinations included height and weight. Participants were weighed at each study visit and any medically significant changes were reported.

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

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to End of Trial (Maximum of 60 weeks)

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

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with Markedly Abnormal ECG Scores

|                 |                                                          |
|-----------------|----------------------------------------------------------|
| End point title | Number of Participants with Markedly Abnormal ECG Scores |
|-----------------|----------------------------------------------------------|

End point description:

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

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to End of Trial (Maximum of 60 weeks)

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

## Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

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

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to End of Trial (Maximum of 60 weeks)

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

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with Markedly Abnormal Laboratory Tests

|                 |                                                                |
|-----------------|----------------------------------------------------------------|
| End point title | Number of Participants with Markedly Abnormal Laboratory Tests |
|-----------------|----------------------------------------------------------------|

End point description:

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

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

|                                                |           |
|------------------------------------------------|-----------|
| End point type                                 | Secondary |
| End point timeframe:                           |           |
| Baseline to End of Trial (Maximum of 60 weeks) |           |

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

## Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The C-SSRS is an assessment tool that evaluates suicidal ideation and behavior. Number of participants with suicidal ideation or behavior was defined as the number of participants who answered "yes" at any time during the treatment period (Baseline to Week 52) to one of the 10 categories:

Category 1: Wish to be dead

Category 2: Non-specific active suicidal thoughts

Category 3: Active suicidal ideation with any methods (not plan) without intent to act

Category 4: Active suicidal ideation with some intent to act, without specific plan

Category 5: Active suicidal ideation with specific plan and intent

Category 6: Preparatory acts or behavior

Category 7: Aborted attempt

Category 8: Interrupted attempt

Category 9: Actual attempt (non-fatal)

Category 10: Completed suicide

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Baseline to Week 52  |           |

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

## Statistical analyses

No statistical analyses for this end point

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

|                                                                                                                                                                                                                                                                                                                             |                                                                                        |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                             | Change from Baseline in Personal Health Questionnaire Depression Scale-8 (PHQ-8) Score |
| End point description:<br>PHQ-8 is a 8-item self-report scale, all items are rated on a score of 0-3, for a total range of 0-24. PHQ-8 assesses symptoms of depression over the previous 2 weeks. Higher scores indicate more depressive symptoms. A negative change from baseline score indicates improvement in symptoms. |                                                                                        |
| End point type                                                                                                                                                                                                                                                                                                              | Secondary                                                                              |
| End point timeframe:<br>Baseline to Week 52                                                                                                                                                                                                                                                                                 |                                                                                        |

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

## Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

Reduction from baseline of  $\geq 4$  points in the SLEDAI-2K

No new organ systems affected, defined by 1 or more BILAG-2004 A or 2 or more BILAG-2004 B items

No worsening from baseline in lupus disease activity. Worsening defined as an increase of  $\geq 0.30$  points on a 3-point PGA VAS

No discontinuation of investigational product and no use of restricted medications beyond the revised post-hoc allowed threshold.

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

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

|                      |          |
|----------------------|----------|
| End point type       | Post-hoc |
| End point timeframe: |          |
| Week 52              |          |

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

## Statistical analyses

|                                   |                                  |
|-----------------------------------|----------------------------------|
| <b>Statistical analysis title</b> | Analysis of Treatment Difference |
|-----------------------------------|----------------------------------|

Statistical analysis description:

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

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

Notes:

[7] - Nominal p-value

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

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

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

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

End point description:

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

Reduction from baseline of  $\geq 4$  points in the SLEDAI-2K

No new organ systems affected, defined by 1 or more BILAG-2004 A or 2 or more BILAG-2004 B items

No worsening from baseline in lupus disease activity. Worsening defined as an increase of  $\geq 0.30$  points on a 3-point PGA VAS

No discontinuation of investigational product and no use of restricted medications beyond the revised post-hoc analysis threshold.

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

|                |          |
|----------------|----------|
| End point type | Post-hoc |
|----------------|----------|

End point timeframe:

Week 52

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

**Statistical analyses**

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



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

Notes:

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

[9] - Nominal p-value

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

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

End point description:

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

Achieve an OCS dose of  $\leq 7.5$  mg/day prednisone or equivalent by Week 40

Maintain an OCS dose  $\leq 7.5$  mg/day prednisone or equivalent from Week 40 to Week 52

No discontinuation of investigational product and no use of restricted medications beyond the revised post-hoc analysis threshold.

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

|                      |          |
|----------------------|----------|
| End point type       | Post-hoc |
| End point timeframe: |          |
| Week 52              |          |

| <b>End point values</b>     | Anifrolumab<br>150 mg<br>Baseline OCS<br>$\geq 10$ mg/day | Anifrolumab<br>300 mg<br>Baseline OCS<br>$\geq 10$ mg/day | Placebo<br>Baseline OCS<br>$\geq 10$ mg/day |  |
|-----------------------------|-----------------------------------------------------------|-----------------------------------------------------------|---------------------------------------------|--|
| Subject group type          | Subject analysis set                                      | Subject analysis set                                      | Subject analysis set                        |  |
| Number of subjects analysed | 48                                                        | 103                                                       | 102                                         |  |
| Units: Participants         | 24                                                        | 50                                                        | 33                                          |  |

### **Statistical analyses**

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

Notes:

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

[11] - Nominal p-value

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

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

End point description:

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

Achieve  $\geq 50\%$  reduction of CLASI activity score at Week 12 compared to baseline

No discontinuation of investigational product and no use of restricted medications beyond the revised post-hoc analysis threshold before assessment.

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

|                      |          |
|----------------------|----------|
| End point type       | Post-hoc |
| End point timeframe: |          |
| Week 12              |          |

| <b>End point values</b>     | Anifrolumab 150 mg CLASI Activity Score $\geq 10$ | Anifrolumab 300 mg CLASI Activity Score $\geq 10$ | Placebo CLASI Activity Score $\geq 10$ |  |
|-----------------------------|---------------------------------------------------|---------------------------------------------------|----------------------------------------|--|
| Subject group type          | Subject analysis set                              | Subject analysis set                              | Subject analysis set                   |  |
| Number of subjects analysed | 30                                                | 58                                                | 54                                     |  |
| Units: Participants         | 16                                                | 25                                                | 14                                     |  |

## Statistical analyses

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

Notes:

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

[13] - Nominal p-value

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

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

End point description:

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

Reduction from baseline of  $\geq 4$  points in the SLEDAI-2K

No new organ systems affected, defined by 1 or more BILAG-2004 A or 2 or more BILAG-2004 B items

No worsening from baseline in lupus disease activity. Worsening defined as an increase of  $\geq 0.30$  points on a 3-point PGA VAS

No discontinuation of investigational product and no use of restricted medications beyond the revised post-hoc allowed threshold.

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

|                      |          |
|----------------------|----------|
| End point type       | Post-hoc |
| End point timeframe: |          |
| Week 24              |          |

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

## Statistical analyses

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

Notes:

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

[15] - Nominal p-value

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

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

End point description:

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

All criteria related to SRI(4) (please see primary endpoint) plus:

Reduction of all baseline BILAG-2004 A to B/C/D and baseline BILAG-2004 B to C/D, and no BILAG-2004 worsening in other organ systems, as defined by 1 or more BILAG-2004 A or 1 or more new BILAG-2004 B item

No discontinuation of investigational product and no use of restricted medications beyond the revised post-hoc analysis threshold before assessment.

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

|                      |          |
|----------------------|----------|
| End point type       | Post-hoc |
| End point timeframe: |          |
| Week 52              |          |

| <b>End point values</b>     | Anifrolumab<br>150 mg | Anifrolumab<br>300 mg | Placebo         |  |
|-----------------------------|-----------------------|-----------------------|-----------------|--|
| Subject group type          | Reporting group       | Reporting group       | Reporting group |  |
| Number of subjects analysed | 93                    | 180                   | 184             |  |
| Units: Participants         | 35                    | 83                    | 54              |  |

## Statistical analyses

| <b>Statistical analysis title</b>                                                                                                                                                                                                                                                                                                                                              | Analysis of Treatment Difference |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|
| Statistical analysis description:                                                                                                                                                                                                                                                                                                                                              |                                  |
| The difference in estimates and associated 95% CI are weighted and are calculated using a stratified Cochran-Mantel-Haenszel (CMH) approach, with stratification factors (SLEDAI-2K score at screening [<10 points vs ≥ 10 points], Week 0 OCS dose [<10 mg/day vs ≥10 mg/day prednisone or equivalent] and type I IFN gene signature test result at screening [high vs low]). |                                  |
| Comparison groups                                                                                                                                                                                                                                                                                                                                                              | Anifrolumab 300 mg v Placebo     |
| Number of subjects included in analysis                                                                                                                                                                                                                                                                                                                                        | 364                              |
| Analysis specification                                                                                                                                                                                                                                                                                                                                                         | Pre-specified                    |
| Analysis type                                                                                                                                                                                                                                                                                                                                                                  | superiority                      |
| Parameter estimate                                                                                                                                                                                                                                                                                                                                                             | Difference in proportions        |
| Point estimate                                                                                                                                                                                                                                                                                                                                                                 | 16.4                             |
| Confidence interval                                                                                                                                                                                                                                                                                                                                                            |                                  |
| level                                                                                                                                                                                                                                                                                                                                                                          | 95 %                             |
| sides                                                                                                                                                                                                                                                                                                                                                                          | 2-sided                          |
| lower limit                                                                                                                                                                                                                                                                                                                                                                    | 6.7                              |
| upper limit                                                                                                                                                                                                                                                                                                                                                                    | 26.2                             |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline to End of Trial (Maximum of 60 weeks post first dose)

Adverse event reporting additional description:

AEs were either spontaneously reported by the participant or reported in response to open questions, revealed by observation, or were changes from baseline/deterioration in tests and vital signs that met SAE criteria or led to IP discontinuation. Full analysis set: All participants who had received at least one dose of investigational product.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 21.0 |
|--------------------|------|

### Reporting groups

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Anifrolumab 150 mg |
|-----------------------|--------------------|

Reporting group description:

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

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Anifrolumab 300 mg |
|-----------------------|--------------------|

Reporting group description:

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

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

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

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

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

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



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

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

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

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

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

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

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

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



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

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

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

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

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

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

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

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

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

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



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

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

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported