



## Clinical trial results:

**A Phase 2, randomized, double-blind, placebo-controlled, multiple ascending dose study to evaluate the efficacy and safety of CAM-3001 in participants with rheumatoid arthritis (RA).**

### Summary

|                          |                      |
|--------------------------|----------------------|
| EudraCT number           | 2009-014735-20       |
| Trial protocol           | LV EE HU CZ LT PL BG |
| Global end of trial date | 27 July 2012         |

### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 07 January 2017 |
| First version publication date | 07 January 2017 |

### Trial information

#### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | MI-CP219 |
|-----------------------|----------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01050998 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | MedImmune, LLC  |
| Sponsor organisation address | Milstein Building, Granta Park, Cambridge, CB21 6GH United Kingdom, United Kingdom,                   |
| Public contact               | Marius Albulescu, Associate Medical Director, MedImmune, LLC, +1 3013980000, albulescum@medimmune.com |
| Scientific contact           | Marius Albulescu, Associate Medical Director, MedImmune, LLC, +1 3013980000, albulescum@medimmune.com |

Notes:

### Paediatric regulatory details

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

Notes:

## Results analysis stage

|  |              |
|--|--------------|
| Analysis stage                                       | Final        |
| Date of interim/final analysis                       | 27 July 2012 |
| Is this the analysis of the primary completion data? | No           |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 27 July 2012 |
| Was the trial ended prematurely?                     | No           |

Notes:

## General information about the trial

Main objective of the trial:

Primary objectives of this study were to evaluate the safety, tolerability, and efficacy of multiple doses of mavrilimumab administered subcutaneous (SC) in participants with at least moderately active rheumatoid arthritis (RA).

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 11 February 2010 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Bulgaria: 25           |
| Country: Number of subjects enrolled | Czech Republic: 22     |
| Country: Number of subjects enrolled | Estonia: 12            |
| Country: Number of subjects enrolled | Japan: 51              |
| Country: Number of subjects enrolled | Latvia: 9              |
| Country: Number of subjects enrolled | Lithuania: 14          |
| Country: Number of subjects enrolled | Poland: 29             |
| Country: Number of subjects enrolled | Romania: 7             |
| Country: Number of subjects enrolled | Russian Federation: 63 |
| Country: Number of subjects enrolled | Ukraine: 28            |
| Country: Number of subjects enrolled | Hungary: 24            |
| Worldwide total number of subjects   | 284                    |
| EEA total number of subjects         | 142                    |

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)                      | 247 |
| From 65 to 84 years                       | 37  |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 516 participants were screened out of which 290 participants were randomized in the study. Six participants from one of the sites were excluded from ITT population prior to unblinding due to data integrity issues.

### Period 1

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

### Arms

|                              |                                |
|------------------------------|--------------------------------|
| Are arms mutually exclusive? | Yes                            |
| <b>Arm title</b>             | Mavrilimumab 10 milligram (mg) |

Arm description:

Participants received Mavrilimumab (CAM-3001) 10 mg injection subcutaneously every other week for 12 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) orally or parenterally.

|  |                  |
|--|------------------|
| Arm type                               | Experimental     |
| Investigational medicinal product name | Mavrilimumab     |
| Investigational medicinal product code | CAM-3001         |
| Other name                             |                  |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

Participants received Mavrilimumab (CAM-3001) 10 milligram (mg) injection subcutaneously every other week for 12 weeks.

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | Mavrilimumab 30 mg |
|------------------|--------------------|

Arm description:

Participants received Mavrilimumab (CAM-3001) 30 mg injection subcutaneously every other week for 12 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) orally or parenterally.

|  |                  |
|--|------------------|
| Arm type                               | Experimental     |
| Investigational medicinal product name | Mavrilimumab     |
| Investigational medicinal product code | CAM-3001         |
| Other name                             |                  |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

Participants received Mavrilimumab (CAM-3001) 30 milligram (mg) injection subcutaneously every other week for 12 weeks.

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | Mavrilimumab 50 mg |
|------------------|--------------------|

Arm description:

Participants received Mavrilimumab (CAM-3001) 50 mg injection subcutaneously every other week for 12 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) orally or parenterally.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|  |                  |
|--|------------------|
| Investigational medicinal product name | Mavrilimumab     |
| Investigational medicinal product code | CAM-3001         |
| Other name                             |                  |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

Participants received Mavrilimumab (CAM-3001) 50 mg injection subcutaneously every other week for 12 weeks.

|                  |                     |
|------------------|---------------------|
| <b>Arm title</b> | Mavrilimumab 100 mg |
|------------------|---------------------|

Arm description:

Participants received Mavrilimumab (CAM-3001) 100 mg injection subcutaneously every other week for 12 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) orally or parenterally.

|  |                  |
|--|------------------|
| Arm type                               | Experimental     |
| Investigational medicinal product name | Mavrilimumab     |
| Investigational medicinal product code | CAM-3001         |
| Other name                             |                  |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

Participants received Mavrilimumab (CAM-3001) 100 mg injection subcutaneously every other week for 12 weeks.

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

Arm description:

Participants received Placebo matched to mavrilimumab injection subcutaneously every other week for 12 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) orally or parenterally.

|  |                  |
|--|------------------|
| Arm type                               | Placebo          |
| Investigational medicinal product name | Placebo          |
| Investigational medicinal product code |                  |
| Other name                             |                  |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

Participants received Placebo Matched to Mavrilimumab injection subcutaneously every other week for 12 weeks.

| Number of subjects in period 1 | Mavrilimumab 10 milligram (mg) | Mavrilimumab 30 mg | Mavrilimumab 50 mg |
|--------------------------------|--------------------------------|--------------------|--------------------|
| Started                        | 48                             | 49                 | 48                 |
| Completed                      | 44                             | 47                 | 46                 |
| Not completed                  | 4                              | 2                  | 2                  |
| Consent withdrawn by subject   | -                              | -                  | -                  |
| Adverse event, non-fatal       | 1                              | -                  | 1                  |
| Unspecified                    | 3                              | 2                  | 1                  |

| Number of subjects in period 1 | Mavrilimumab 100 mg | Placebo |
|--------------------------------|---------------------|---------|
| Started                        | 47                  | 92      |

|                              |    |    |
|------------------------------|----|----|
| Completed                    | 45 | 82 |
| Not completed                | 2  | 10 |
| Consent withdrawn by subject | 1  | 3  |
| Adverse event, non-fatal     | -  | 2  |
| Unspecified                  | 1  | 5  |

## Baseline characteristics

### Reporting groups

|  |                                |
|--|--------------------------------|
| Reporting group title  | Mavrilimumab 10 milligram (mg) |
| Reporting group description:<br>Participants received Mavrilimumab (CAM-3001) 10 mg injection subcutaneously every other week for 12 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) orally or parenterally.   |                                |
| Reporting group title  | Mavrilimumab 30 mg             |
| Reporting group description:<br>Participants received Mavrilimumab (CAM-3001) 30 mg injection subcutaneously every other week for 12 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) orally or parenterally.   |                                |
| Reporting group title  | Mavrilimumab 50 mg             |
| Reporting group description:<br>Participants received Mavrilimumab (CAM-3001) 50 mg injection subcutaneously every other week for 12 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) orally or parenterally.   |                                |
| Reporting group title  | Mavrilimumab 100 mg            |
| Reporting group description:<br>Participants received Mavrilimumab (CAM-3001) 100 mg injection subcutaneously every other week for 12 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) orally or parenterally.  |                                |
| Reporting group title  | Placebo                        |
| Reporting group description:<br>Participants received Placebo matched to mavrilimumab injection subcutaneously every other week for 12 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) orally or parenterally. |                                |

| Reporting group values                     | Mavrilimumab 10 milligram (mg) | Mavrilimumab 30 mg | Mavrilimumab 50 mg |
|--|--------------------------------|--------------------|--------------------|
| Number of subjects                         | 48                             | 49                 | 48                 |
| Age categorical<br>Units: Subjects         |                                |                    |                    |
| Adults (18- 64 Years)                      | 42                             | 43                 | 42                 |
| Elderly (65-84 Years)                      | 6                              | 6                  | 6                  |
| Age Continuous  <br>Units: years           |                                |                    |                    |
| arithmetic mean                            | 52.2                           | 51.1               | 52.7               |
| standard deviation                         | ± 11.9                         | ± 12.1             | ± 10.3             |
| Gender, Male/Female<br>Units: participants |                                |                    |                    |
| Female                                     | 39                             | 43                 | 44                 |
| Male                                       | 9                              | 6                  | 4                  |

| Reporting group values             | Mavrilimumab 100 mg | Placebo | Total |
|------------------------------------|---------------------|---------|-------|
| Number of subjects                 | 47                  | 92      | 284   |
| Age categorical<br>Units: Subjects |                     |         |       |
| Adults (18- 64 Years)              | 42                  | 78      | 247   |
| Elderly (65-84 Years)              | 5                   | 14      | 37    |

|   |                |                |     |
|---|----------------|----------------|-----|
| Age Continuous  <br>Units: years<br>arithmetic mean<br>standard deviation | 50.1<br>± 12.1 | 52.1<br>± 12.8 | -   |
| Gender, Male/Female<br>Units: participants                                |                |                |     |
| Female  | 40             | 82             | 248 |
| Male  | 7              | 10             | 36  |



## End points

### End points reporting groups

|  |                                |
|--|--------------------------------|
| Reporting group title  | Mavrilimumab 10 milligram (mg) |
| Reporting group description:<br>Participants received Mavrilimumab (CAM-3001) 10 mg injection subcutaneously every other week for 12 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) orally or parenterally.       |                                |
| Reporting group title  | Mavrilimumab 30 mg             |
| Reporting group description:<br>Participants received Mavrilimumab (CAM-3001) 30 mg injection subcutaneously every other week for 12 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) orally or parenterally.       |                                |
| Reporting group title  | Mavrilimumab 50 mg             |
| Reporting group description:<br>Participants received Mavrilimumab (CAM-3001) 50 mg injection subcutaneously every other week for 12 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) orally or parenterally.       |                                |
| Reporting group title  | Mavrilimumab 100 mg            |
| Reporting group description:<br>Participants received Mavrilimumab (CAM-3001) 100 mg injection subcutaneously every other week for 12 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) orally or parenterally.      |                                |
| Reporting group title  | Placebo                        |
| Reporting group description:<br>Participants received Placebo matched to mavrilimumab injection subcutaneously every other week for 12 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) orally or parenterally.     |                                |
| Subject analysis set title   | Placebo                        |
| Subject analysis set type  | Safety analysis                |
| Subject analysis set description:<br>Placebo matched to mavrilimumab injection subcutaneously every other week for 12 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) orally or parenterally.                      |                                |
| Subject analysis set title   | Mavrilimumab 50 mg             |
| Subject analysis set type  | Safety analysis                |
| Subject analysis set description:<br>Participants received Mavrilimumab (CAM-3001) 50 mg injection subcutaneously every other week for 12 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) orally or parenterally.  |                                |
| Subject analysis set title   | Mavrilimumab 100mg             |
| Subject analysis set type  | Safety analysis                |
| Subject analysis set description:<br>Participants received Mavrilimumab (CAM-3001) 100 mg injection subcutaneously every other week for 12 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) orally or parenterally. |                                |

### Primary: Percentage of Participants who Achieved Disease Activity Score of 28 Joints Using C-Reactive Protein (DAS28 [CRP]) Response at Day 85

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants who Achieved Disease Activity Score of 28 Joints Using C-Reactive Protein (DAS28 [CRP]) Response at Day 85 |
|-----------------|---|

#### End point description:

DAS28 (CRP) calculated swollen joint count (SJC) and tender joint count (TJC) using the 28 joints, general health (GH) using participant assessment of disease activity (participant rated arthritis activity using the numerical rating scale with 0 = best, 10 = worst), and CRP (milligram per Liter [mg/L]). Total score range: 0-9.4, higher score= more disease activity. DAS28 (CRP) less than (<) 3.2 = low disease activity, greater than or equal to (>=) 3.2 to 5.1 = moderate to high disease activity and <2.6=

remission. A Day 85 responder was defined as a participant who experienced more than 1.2 decrease from baseline in DAS28 (CRP) score at Day 85. The intent-to-treat (ITT) population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues.

|                      |         |
|----------------------|---------|
| End point type       | Primary |
| End point timeframe: |         |
| Day 85               |         |

| End point values                  | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|-----------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed       | 48                                   | 49                    | 48                    | 47                     |
| Units: percentage of participants |                                      |                       |                       |                        |
| number (not applicable)           | 37.5                                 | 63.3                  | 47.9                  | 68.1                   |

| End point values                  | Placebo         |  |  |  |
|-----------------------------------|-----------------|--|--|--|
| Subject group type                | Reporting group |  |  |  |
| Number of subjects analysed       | 92              |  |  |  |
| Units: percentage of participants |                 |  |  |  |
| number (not applicable)           | 32.6            |  |  |  |

## Statistical analyses

|   |  |
|---|--|
| Statistical analysis title              | Statistical Analysis 1                   |
| Statistical analysis description:       |  |
| Analysis Type used was dose escalation. |  |
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 140                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[1]</sup>                     |
| P-value                                 | = 0.578 <sup>[2]</sup>                   |
| Method                                  | Fisher exact                             |
| Parameter estimate                      | Percent difference                       |
| Point estimate                          | 4.9                                      |
| Confidence interval                     |  |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | -11.5                                    |
| upper limit                             | 22                                       |

Notes:

[1] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[2] - p-value was calculated using a two-tailed Fisher's exact test.

|  |                        |
|--|------------------------|
|  | Statistical Analysis 2 |
|--|------------------------|

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       |                              |
| Statistical analysis description:       |                              |
| Analysis Type used was dose escalation. |                              |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 141                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[3]</sup>         |
| P-value                                 | < 0.001 <sup>[4]</sup>       |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 30.7                         |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | 13.4                         |
| upper limit                             | 46.3                         |

Notes:

[3] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[4] - p-value was calculated using a two-tailed Fisher's exact test.

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 3       |
| Statistical analysis description:       |                              |
| Analysis Type used was dose escalation. |                              |
| Comparison groups                       | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 140                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[5]</sup>         |
| P-value                                 | = 0.099 <sup>[6]</sup>       |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 15.3                         |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -1.6                         |
| upper limit                             | 32.2                         |

Notes:

[5] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[6] - p-value was calculated using a two-tailed Fisher's exact test.

|   |                               |
|---|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 4        |
| Statistical analysis description:       |                               |
| Analysis Type used was dose escalation. |                               |
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |

|   |                        |
|---|------------------------|
| Number of subjects included in analysis | 139                    |
| Analysis specification                  | Pre-specified          |
| Analysis type                           | other <sup>[7]</sup>   |
| P-value                                 | < 0.001 <sup>[8]</sup> |
| Method                                  | Fisher exact           |
| Parameter estimate                      | Percent difference     |
| Point estimate                          | 35.5                   |
| Confidence interval                     |                        |
| level                                   | 95 %                   |
| sides                                   | 2-sided                |
| lower limit                             | 17.8                   |
| upper limit                             | 50.6                   |

Notes:

[7] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[8] - p-value was calculated using a two-tailed Fisher's exact test.

### **Primary: Percentage of Participants who Achieved Disease Activity Score of 28 Joints Using C-Reactive Protein (DAS28 [CRP]) Response at Day 85 by Region**

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants who Achieved Disease Activity Score of 28 Joints Using C-Reactive Protein (DAS28 [CRP]) Response at Day 85 by Region |
|-----------------|---|

End point description:

DAS28 (CRP) calculated SJC and TJC using the 28 joints, GH using participant assessment of disease activity (participant rated arthritis activity using the numerical rating scale with 0 = best, 10 = worst), and CRP (mg/L). Total score range: 0-9.4, higher score= more disease activity. DAS28 (CRP) <3.2 = low disease activity, >=3.2 to 5.1 = moderate to high disease activity and <2.6= remission. A Day 85 responder was defined as a participant who experienced more than 1.2 decrease from baseline in DAS28 (CRP) score at Day 85. DAS28 (CRP) response at Day 85 for the European and Japanese regions were reported. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues. Here "n" signifies participants who were evaluable for the specified region for each arm, respectively.

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

End point timeframe:

Day 85

| End point values                       | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|--|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                     | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed            | 48                                   | 49                    | 48                    | 47                     |
| Units: percentage of participants      |                                      |                       |                       |                        |
| number (not applicable)                |                                      |                       |                       |                        |
| European Region (n=75, 39, 41, 39, 39) | 41                                   | 61                    | 51.3                  | 66.7                   |
| Japanese Region (n=17, 9, 8, 9, 8)     | 22.2                                 | 75                    | 33.3                  | 75                     |

| End point values            | Placebo         |  |  |  |
|-----------------------------|-----------------|--|--|--|
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 92              |  |  |  |

|  |      |  |  |  |
|--|------|--|--|--|
| Units: percentage of participants      |      |  |  |  |
| number (not applicable)                |      |  |  |  |
| European Region (n=75, 39, 41, 39, 39) | 34.7 |  |  |  |
| Japanese Region (n=17, 9, 8, 9, 8)     | 23.5 |  |  |  |

## Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Statistical Analysis 1                   |
| Statistical analysis description:       |  |
| Analysis Type used was dose escalation. |  |
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 140                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[9]</sup>                     |
| P-value                                 | = 0.543 <sup>[10]</sup>                  |
| Method                                  | Fisher exact                             |
| Parameter estimate                      | Percent difference                       |
| Point estimate                          | 6.4                                      |
| Confidence interval                     |  |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | -11.9                                    |
| upper limit                             | 25.4                                     |

Notes:

[9] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[10] - European region: p-value was calculated using a two-tailed Fisher's exact test.

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 2       |
| Statistical analysis description:       |                              |
| Analysis Type used was dose escalation. |                              |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 141                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[11]</sup>        |
| P-value                                 | = 0.011 <sup>[12]</sup>      |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 26.3                         |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | 7.2                          |
| upper limit                             | 43.6                         |

Notes:

[11] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[12] - European region: p-value was calculated using a two-tailed Fisher's exact test.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 3 |
|-----------------------------------|------------------------|

|   |                              |
|---|------------------------------|
| Statistical analysis description:       |                              |
| Analysis Type used was dose escalation. |                              |
| Comparison groups                       | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 140                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[13]</sup>        |
| P-value                                 | = 0.108 <sup>[14]</sup>      |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 16.6                         |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -2.5                         |
| upper limit                             | 35.5                         |

Notes:

[13] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[14] - European region: p-value was calculated using a two-tailed Fisher's exact test.

|   |                               |
|---|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 4        |
| Statistical analysis description:       |                               |
| Analysis Type used was dose escalation. |                               |
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 139                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[15]</sup>         |
| P-value                                 | = 0.001 <sup>[16]</sup>       |
| Method                                  | Fisher exact                  |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | 32                            |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 12.5                          |
| upper limit                             | 49                            |

Notes:

[15] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[16] - European region: p-value was calculated using a two-tailed Fisher's exact test.

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Statistical Analysis 5                   |
| Statistical analysis description:       |  |
| Analysis Type used was dose escalation. |  |
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 140                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[17]</sup>                    |
| P-value                                 | = 1 <sup>[18]</sup>                      |
| Method                                  | Fisher exact                             |
| Parameter estimate                      | Percent difference                       |
| Point estimate                          | -1.3                                     |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -33.7   |
| upper limit         | 35.7    |

Notes:

[17] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[18] - Japanese region: p-value was calculated using a two-tailed Fisher's exact test.

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Statistical Analysis 6                             |
| Statistical analysis description:       |  |
| Analysis Type used was dose escalation. |  |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 188  |
| Analysis specification                  | Pre-specified                                      |
| Analysis type                           | other <sup>[19]</sup>                              |
| P-value                                 | = 0.028 <sup>[20]</sup>                            |
| Method                                  | Fisher exact                                       |
| Parameter estimate                      | Percent difference                                 |
| Point estimate                          | 51.5   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 8.2  |
| upper limit                             | 77   |

Notes:

[19] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[20] - Japanese region: p-value was calculated using a two-tailed Fisher's exact test.

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 7       |
| Statistical analysis description:       |                              |
| Analysis Type used was dose escalation. |                              |
| Comparison groups                       | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 140                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[21]</sup>        |
| P-value                                 | = 0.661 <sup>[22]</sup>      |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 9.8                          |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -24.3                        |
| upper limit                             | 46.9                         |

Notes:

[21] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[22] - Japanese region: p-value was calculated using a two-tailed Fisher's exact test.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 8 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis Type used was dose escalation.

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 188  |
| Analysis specification                  | Pre-specified                                      |
| Analysis type                           | other <sup>[23]</sup>                              |
| P-value                                 | = 0.028 <sup>[24]</sup>                            |
| Method                                  | Fisher exact                                       |
| Parameter estimate                      | Percent difference                                 |
| Point estimate                          | 51.5   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 8.2  |
| upper limit                             | 77   |

Notes:

[23] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[24] - Japanese region: p-value was calculated using a two-tailed Fisher's exact test.

### **Primary: Percentage of Participants who Achieved Disease Activity Score of 28 Joints Using Erythrocyte Sedimentation Rate (DAS28 [ESR]) at Day 85**

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants who Achieved Disease Activity Score of 28 Joints Using Erythrocyte Sedimentation Rate (DAS28 [ESR]) at Day 85 |
|-----------------|--|

End point description:

DAS28 (ESR) calculated SJC and TJC using the 28 joints, GH using participant assessment of disease activity (participant rated arthritis activity using the numerical rating scale with 0 = best, 10 = worst), and the erythrocyte sedimentation rate (ESR) (millimeters per hour [mm/hour]). Total score range: 0-9.4, higher score = more disease activity. DAS28 (ESR) <3.2 = low disease activity, >=3.2 to 5.1 = moderate to high disease activity and <2.6 = remission. A Day 85 responder was defined as a participant who experienced more than 1.2 decrease from baseline in DAS28 (ESR) score at Day 85. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues.

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

End point timeframe:

Day 85

| End point values                  | Mavrilimumab 10 milligram (mg) | Mavrilimumab 30 mg | Mavrilimumab 50 mg | Mavrilimumab 100 mg |
|-----------------------------------|--------------------------------|--------------------|--------------------|---------------------|
| Subject group type                | Reporting group                | Reporting group    | Reporting group    | Reporting group     |
| Number of subjects analysed       | 48                             | 49                 | 48                 | 47                  |
| Units: percentage of participants |                                |                    |                    |                     |
| number (not applicable)           | 50                             | 61.2               | 58.3               | 66                  |

| End point values            | Placebo         |  |  |  |
|-----------------------------|-----------------|--|--|--|
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 92              |  |  |  |



|                                   |    |  |  |  |
|-----------------------------------|----|--|--|--|
| Units: percentage of participants |    |  |  |  |
| number (not applicable)           | 37 |  |  |  |

## Statistical analyses

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Statistical Analysis 1                   |
| Statistical analysis description:<br>Analysis Type used was dose escalation. |  |
| Comparison groups  | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis                                      | 140                                      |
| Analysis specification   | Pre-specified                            |
| Analysis type  | other <sup>[25]</sup>                    |
| P-value  | = 0.152 <sup>[26]</sup>                  |
| Method   | Fisher exact                             |
| Parameter estimate   | Percent difference                       |
| Point estimate   | 13                                       |
| Confidence interval  |  |
| level  | 95 %                                     |
| sides  | 2-sided                                  |
| lower limit  | -4.2                                     |
| upper limit  | 30.3                                     |

Notes:

[25] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[26] - p-value was calculated using a two-tailed Fisher's exact test.

|  |                              |
|--|------------------------------|
| <b>Statistical analysis title</b>  | Statistical Analysis 2       |
| Statistical analysis description:<br>Analysis Type used was dose escalation. |                              |
| Comparison groups  | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis                                      | 141                          |
| Analysis specification   | Pre-specified                |
| Analysis type  | other <sup>[27]</sup>        |
| P-value  | = 0.008 <sup>[28]</sup>      |
| Method   | Fisher exact                 |
| Parameter estimate   | Percent difference           |
| Point estimate   | 24.3                         |
| Confidence interval  |                              |
| level  | 95 %                         |
| sides  | 2-sided                      |
| lower limit  | 7                            |
| upper limit  | 40.3                         |

Notes:

[27] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[28] - p-value was calculated using a two-tailed Fisher's exact test.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis Type used was dose escalation.

|   |                              |
|---|------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 140                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[29]</sup>        |
| P-value                                 | = 0.02 <sup>[30]</sup>       |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 21.4                         |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | 3.9                          |
| upper limit                             | 37.8                         |

Notes:

[29] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[30] - p-value was calculated using a two-tailed Fisher's exact test.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 139                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[31]</sup>         |
| P-value                                 | = 0.002 <sup>[32]</sup>       |
| Method                                  | Fisher exact                  |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | 29                            |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 11.3                          |
| upper limit                             | 45                            |

Notes:

[31] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[32] - p-value was calculated using a two-tailed Fisher's exact test.

### **Primary: Percentage of Participants who Achieved Disease Activity Score of 28 Joints Using Erythrocyte Sedimentation Rate (DAS28 [ESR]) at Day 85 by Region**

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants who Achieved Disease Activity Score of 28 Joints Using Erythrocyte Sedimentation Rate (DAS28 [ESR]) at Day 85 by Region |
|-----------------|--|

End point description:

DAS28 (ESR) calculated SJC and TJC using the 28 joints, GH using participant assessment of disease activity (participant rated arthritis activity using the numerical rating scale with 0=best, 10=worst), and the erythrocyte sedimentation rate (ESR) (millimeters per hour [mm/hour]). Total score range: 0-9.4, higher score=more disease activity. DAS28 (ESR) <3.2 = low disease activity, >=3.2 to 5.1 = moderate to high disease activity and <2.6= remission. A Day 85 responder was defined as a participant who experienced more than 1.2 decrease from baseline in DAS28 (ESR) score at Day 85. DAS28 (ESR) response at Day 85 for the European and Japanese regions were reported. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues. Here "n"

signifies participants who were evaluable for the specified region for each arm, respectively.

|                      |         |
|----------------------|---------|
| End point type       | Primary |
| End point timeframe: |         |
| Day 85               |         |

| End point values                       | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|--|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                     | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed            | 48                                   | 49                    | 48                    | 47                     |
| Units: percentage of participants      |                                      |                       |                       |                        |
| number (not applicable)                |                                      |                       |                       |                        |
| European Region (n=75, 39, 41, 39, 39) | 51.3                                 | 58.5                  | 61.5                  | 64.1                   |
| Japanese Region (n=17, 9, 8, 9, 8)     | 44.4                                 | 75                    | 44.4                  | 75                     |

| End point values                       | Placebo         |  |  |  |
|--|-----------------|--|--|--|
| Subject group type                     | Reporting group |  |  |  |
| Number of subjects analysed            | 92              |  |  |  |
| Units: percentage of participants      |                 |  |  |  |
| number (not applicable)                |                 |  |  |  |
| European Region (n=75, 39, 41, 39, 39) | 41.3            |  |  |  |
| Japanese Region (n=17, 9, 8, 9, 8)     | 17.6            |  |  |  |

## Statistical analyses

|   |  |
|---|--|
| Statistical analysis title              | Statistical Analysis 1                   |
| Statistical analysis description:       |  |
| Analysis Type used was dose escalation. |  |
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 140                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[33]</sup>                    |
| P-value                                 | = 0.328 <sup>[34]</sup>                  |
| Method                                  | Fisher exact                             |
| Parameter estimate                      | Percent difference                       |
| Point estimate                          | 9.9                                      |
| Confidence interval                     |  |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | -9.3                                     |
| upper limit                             | 29.4                                     |

Notes:

[33] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[34] - European region: p-value was calculated using a two-tailed Fisher's exact test.

|  |                              |
|--|------------------------------|
| <b>Statistical analysis title</b>  | Statistical Analysis 2       |
| Statistical analysis description:<br>Analysis Type used was dose escalation. |                              |
| Comparison groups  | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis                                      | 141                          |
| Analysis specification   | Pre-specified                |
| Analysis type  | other <sup>[35]</sup>        |
| P-value  | = 0.084 <sup>[36]</sup>      |
| Method   | Fisher exact                 |
| Parameter estimate   | Percent difference           |
| Point estimate   | 17.2                         |
| Confidence interval  |                              |
| level  | 95 %                         |
| sides  | 2-sided                      |
| lower limit  | -2                           |
| upper limit  | 35.6                         |

Notes:

[35] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[36] - European region: p-value was calculated using a two-tailed Fisher's exact test.

|  |                              |
|--|------------------------------|
| <b>Statistical analysis title</b>  | Statistical Analysis 3       |
| Statistical analysis description:<br>Analysis Type used was dose escalation. |                              |
| Comparison groups  | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis                                      | 140                          |
| Analysis specification   | Pre-specified                |
| Analysis type  | other <sup>[37]</sup>        |
| P-value  | = 0.049 <sup>[38]</sup>      |
| Method   | Fisher exact                 |
| Parameter estimate   | Percent difference           |
| Point estimate   | 20.2                         |
| Confidence interval  |                              |
| level  | 95 %                         |
| sides  | 2-sided                      |
| lower limit  | 0.7                          |
| upper limit  | 38.2                         |

Notes:

[37] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[38] - European region: p-value was calculated using a two-tailed Fisher's exact test.

|  |                               |
|--|-------------------------------|
| <b>Statistical analysis title</b>  | Statistical Analysis 4        |
| Statistical analysis description:<br>Analysis Type used was dose escalation. |                               |
| Comparison groups  | Placebo v Mavrilimumab 100 mg |

|   |                        |
|---|------------------------|
| Number of subjects included in analysis | 139                    |
| Analysis specification                  | Pre-specified          |
| Analysis type                           | other <sup>[39]</sup>  |
| P-value                                 | = 0.03 <sup>[40]</sup> |
| Method                                  | Fisher exact           |
| Parameter estimate                      | Percent difference     |
| Point estimate                          | 22.8                   |
| Confidence interval                     |                        |
| level                                   | 95 %                   |
| sides                                   | 2-sided                |
| lower limit                             | 3.2                    |
| upper limit                             | 40.7                   |

Notes:

[39] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[40] - European region: p-value was calculated using a two-tailed Fisher's exact test.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 5 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis Type used was dose escalation.

|   |   |
|---|---|
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 188   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other <sup>[41]</sup>   |
| P-value                                 | = 0.188 <sup>[42]</sup>                                       |
| Method                                  | Fisher exact  |
| Parameter estimate                      | Percent difference  |
| Point estimate                          | 26.8  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -9.3  |
| upper limit                             | 60.7  |

Notes:

[41] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[42] - Japanese region: p-value was calculated using a two-tailed Fisher's exact test.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 6 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis Type used was dose escalation.

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 188  |
| Analysis specification                  | Pre-specified                                      |
| Analysis type                           | other <sup>[43]</sup>                              |
| P-value                                 | = 0.01 <sup>[44]</sup>                             |
| Method                                  | Fisher exact                                       |
| Parameter estimate                      | Percent difference                                 |
| Point estimate                          | 57.4   |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 15.2    |
| upper limit         | 81.8    |

Notes:

[43] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[44] - Japanese region: p-value was calculated using a two-tailed Fisher's exact test.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Statistical Analysis 7  |
| Statistical analysis description:       |   |
| Analysis Type used was dose escalation. |   |
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 188   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other <sup>[45]</sup>   |
| P-value                                 | = 0.188 <sup>[46]</sup>                                       |
| Method                                  | Fisher exact  |
| Parameter estimate                      | Percent difference  |
| Point estimate                          | 26.8  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -9.3  |
| upper limit                             | 60.7  |

Notes:

[45] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[46] - Japanese region: p-value was calculated using a two-tailed Fisher's exact test.

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Statistical Analysis 8                             |
| Statistical analysis description:       |  |
| Analysis Type used was dose escalation. |  |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 188  |
| Analysis specification                  | Pre-specified                                      |
| Analysis type                           | other <sup>[47]</sup>                              |
| P-value                                 | = 0.01 <sup>[48]</sup>                             |
| Method                                  | Fisher exact                                       |
| Parameter estimate                      | Percent difference                                 |
| Point estimate                          | 57.4   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 15.2   |
| upper limit                             | 81.8   |

Notes:

[47] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[48] - Japanese region: p-value was calculated using a two-tailed Fisher's exact test.

## Primary: Percentage of Participants who Achieved DAS28 (CRP) Response by

## European League Against Rheumatism (EULAR) Category at Day 85

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants who Achieved DAS28 (CRP) Response by European League Against Rheumatism (EULAR) Category at Day 85 <sup>[49]</sup> |
|-----------------|---|

End point description:

DAS28 (CRP) response by EULAR category were used to measure individual response as none, moderate, and good, depending on the extent of change from baseline and the level of disease activity reached. Good response: change from baseline more than ( $>$ )1.2 but less than ( $<$ ) 3.2; moderate response: change from baseline  $>$ 1.2 to more than or equal to ( $\geq$ ) 3.2 or less than or equal to ( $\leq$ ) 5.1 or change from baseline  $\geq$ 0.6 to  $\leq$  1.2 to  $\geq$ 3.2 to  $\leq$ 5.1; no response: change from baseline  $<$ 0.6 or change from baseline  $\geq$ 0.6 and  $\leq$ 1.2 to  $>$ 5.1. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues.

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

End point timeframe:

Day 85

Notes:

[49] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

| End point values                  | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|-----------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed       | 48                                   | 49                    | 48                    | 47                     |
| Units: percentage of participants |                                      |                       |                       |                        |
| number (not applicable)           |                                      |                       |                       |                        |
| No response                       | 47.9                                 | 28.6                  | 35.4                  | 23.4                   |
| Moderate response                 | 31.3                                 | 38.8                  | 41.7                  | 42.6                   |
| Good response                     | 20.8                                 | 32.7                  | 22.9                  | 34                     |

| End point values                  | Placebo         |  |  |  |
|-----------------------------------|-----------------|--|--|--|
| Subject group type                | Reporting group |  |  |  |
| Number of subjects analysed       | 92              |  |  |  |
| Units: percentage of participants |                 |  |  |  |
| number (not applicable)           |                 |  |  |  |
| No response                       | 51.1            |  |  |  |
| Moderate response                 | 34.8            |  |  |  |
| Good response                     | 14.1            |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Participants who Achieved DAS28 (CRP) Response by European League Against Rheumatism (EULAR) Category at Day 85 by Region

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants who Achieved DAS28 (CRP) Response by European League Against Rheumatism (EULAR) Category at Day 85 by Region <sup>[50]</sup> |
|-----------------|---|

End point description:

DAS28 (CRP) response by EULAR category were used to measure individual response as none, moderate, and good, depending on the extent of change from baseline and the level of disease activity reached. Good response: change from baseline more than ( $>$ )1.2 but less than ( $<$ ) 3.2; moderate response: change from baseline  $>1.2$  to more than or equal to ( $\geq$ ) 3.2 or less than or equal to ( $\leq$ ) 5.1 or change from baseline  $\geq 0.6$  to  $\leq 1.2$  to  $\geq 3.2$  to  $\leq 5.1$ ; no response: change from baseline  $<0.6$  or change from baseline  $\geq 0.6$  and  $\leq 1.2$  to  $>5.1$ . The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues. Here "n" signifies participants who were evaluable for the specified region for each arm, respectively.

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

End point timeframe:

Day 85

Notes:

[50] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

| End point values                                  | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|---|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                                | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed                       | 48                                   | 49                    | 48                    | 47                     |
| Units: percentage of participants                 |                                      |                       |                       |                        |
| number (not applicable)                           |                                      |                       |                       |                        |
| European: No response<br>(n=75,39,41,39,39)       | 46.2                                 | 29.3                  | 33.3                  | 23.1                   |
| European: Moderate response<br>(n=75,39,41,39,39) | 33.3                                 | 41.5                  | 41                    | 46.2                   |
| European: Good response<br>(n=75,39,41,39,39)     | 20.5                                 | 29.3                  | 25.6                  | 30.8                   |
| Japanese: No response (n=17,9,8,9,8)              | 55.6                                 | 25                    | 44.4                  | 25                     |
| Japanese: Moderate response<br>(n=17,9,8,9,8)     | 22.2                                 | 25                    | 44.4                  | 25                     |
| Japanese: Good response<br>(n=17,9,8,9,8)         | 22.2                                 | 50                    | 11.1                  | 50                     |

| End point values                                  | Placebo         |  |  |  |
|---|-----------------|--|--|--|
| Subject group type                                | Reporting group |  |  |  |
| Number of subjects analysed                       | 92              |  |  |  |
| Units: percentage of participants                 |                 |  |  |  |
| number (not applicable)                           |                 |  |  |  |
| European: No response<br>(n=75,39,41,39,39)       | 49.3            |  |  |  |
| European: Moderate response<br>(n=75,39,41,39,39) | 36              |  |  |  |
| European: Good response<br>(n=75,39,41,39,39)     | 14.7            |  |  |  |
| Japanese: No response (n=17,9,8,9,8)              | 58.8            |  |  |  |
| Japanese: Moderate response<br>(n=17,9,8,9,8)     | 29.4            |  |  |  |
| Japanese: Good response<br>(n=17,9,8,9,8)         | 11.8            |  |  |  |



## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of Participants who Achieved DAS28 (ESR) Response by European League Against Rheumatism (EULAR) Category at Day 85

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants who Achieved DAS28 (ESR) Response by European League Against Rheumatism (EULAR) Category at Day 85 <sup>[51]</sup> |
|-----------------|---|

End point description:

DAS28 (CRP) response by EULAR category were used to measure individual response as none, moderate, and good, depending on the extent of change from baseline and the level of disease activity reached. Good response: change from baseline more than ( $>$ ) 1.2 but less than ( $<$ ) 3.2; moderate response: change from baseline  $>$  1.2 to more than or equal to ( $\geq$ ) 3.2 or less than or equal to ( $\leq$ ) 5.1 or change from baseline  $\geq$  0.6 to  $\leq$  1.2 to  $\geq$  3.2 to  $\leq$  5.1; no response: change from baseline  $<$  0.6 or change from baseline  $\geq$  0.6 and  $\leq$  1.2 to  $>$  5.1. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues.

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

End point timeframe:

Day 85

Notes:

[51] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

| End point values                  | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|-----------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed       | 48                                   | 49                    | 48                    | 47                     |
| Units: percentage of participants |                                      |                       |                       |                        |
| number (not applicable)           |                                      |                       |                       |                        |
| No response                       | 39.6                                 | 36.7                  | 33.3                  | 25.5                   |
| Moderate response                 | 45.8                                 | 44.9                  | 54.2                  | 53.2                   |
| Good response                     | 14.6                                 | 18.4                  | 12.5                  | 21.3                   |

| End point values                  | Placebo         |  |  |  |
|-----------------------------------|-----------------|--|--|--|
| Subject group type                | Reporting group |  |  |  |
| Number of subjects analysed       | 92              |  |  |  |
| Units: percentage of participants |                 |  |  |  |
| number (not applicable)           |                 |  |  |  |
| No response                       | 55.4            |  |  |  |
| Moderate response                 | 35.9            |  |  |  |
| Good response                     | 8.7             |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of Participants who Achieved DAS28 (ESR) Response by European League Against Rheumatism (EULAR) Category at Day 85 by Region

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants who Achieved DAS28 (ESR) Response by European League Against Rheumatism (EULAR) Category at Day 85 by Region <sup>[52]</sup> |
|-----------------|---|

End point description:

DAS28 (CRP) response by EULAR category were used to measure individual response as none, moderate, and good, depending on the extent of change from baseline and the level of disease activity reached. Good response: change from baseline more than ( $>$ ) 1.2 but less than ( $<$ ) 3.2; moderate response: change from baseline  $>$  1.2 to more than or equal to ( $\geq$ ) 3.2 or less than or equal to ( $\leq$ ) 5.1 or change from baseline  $\geq$  0.6 to  $\leq$  1.2 to  $\geq$  3.2 to  $\leq$  5.1; no response: change from baseline  $<$  0.6 or change from baseline  $\geq$  0.6 and  $\leq$  1.2 to  $>$  5.1. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues. Here "n" signifies participants who were evaluable for the specified region for each arm, respectively.

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

End point timeframe:

Day 85

Notes:

[52] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

| End point values                                  | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|---|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                                | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed                       | 48                                   | 49                    | 48                    | 47                     |
| Units: percentage of participants                 |                                      |                       |                       |                        |
| number (not applicable)                           |                                      |                       |                       |                        |
| European: No response<br>(n=75,39,41,39,39)       | 38.5                                 | 39                    | 33.3                  | 28.2                   |
| European: Moderate response<br>(n=75,39,41,39,39) | 46.2                                 | 43.9                  | 53.8                  | 51.3                   |
| European: Good response<br>(n=75,39,41,39,39)     | 15.4                                 | 17.1                  | 12.8                  | 20.5                   |
| Japanese: No response (n=17,9,8,9,8)              | 44.4                                 | 25                    | 33.3                  | 12.5                   |
| Japanese: Moderate response<br>(n=17,9,8,9,8)     | 44.4                                 | 50                    | 55.6                  | 62.5                   |
| Japanese: Good response<br>(n=17,9,8,9,8)         | 11.1                                 | 25                    | 11.1                  | 25                     |

|                  |         |  |  |  |
|------------------|---------|--|--|--|
| End point values | Placebo |  |  |  |
|------------------|---------|--|--|--|

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| Subject group type                                | Reporting group |  |  |  |
| Number of subjects analysed                       | 92              |  |  |  |
| Units: percentage of participants                 |                 |  |  |  |
| number (not applicable)                           |                 |  |  |  |
| European: No response<br>(n=75,39,41,39,39)       | 53.3            |  |  |  |
| European: Moderate response<br>(n=75,39,41,39,39) | 38.7            |  |  |  |
| European: Good response<br>(n=75,39,41,39,39)     | 8               |  |  |  |
| Japanese: No response (n=17,9,8,9,8)              | 64.7            |  |  |  |
| Japanese: Moderate response<br>(n=17,9,8,9,8)     | 23.5            |  |  |  |
| Japanese: Good response<br>(n=17,9,8,9,8)         | 11.8            |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs)

|                 |  |
|-----------------|--|
| End point title | Number of Participants With Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs) <sup>[53]</sup> <sup>[54]</sup> |
|-----------------|--|

End point description:

An adverse event (AE) was any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. An SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent are events between first dose of study drug and up Day 169 that were absent before treatment or that worsened relative to pretreatment state. The safety population included all participants who received any dose of investigational product.

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

End point timeframe:

Baseline up to Day 169 (follow-up)

Notes:

[53] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

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

Justification: The subject analysis sets were created for the safety population due to difference in evaluable participants for the reporting groups and data has been represented accordingly; hence not all the baseline period arms included while reporting end point data.

| End point values            | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Placebo              | Mavrilimumab<br>50 mg |
|-----------------------------|--------------------------------------|-----------------------|----------------------|-----------------------|
| Subject group type          | Reporting group                      | Reporting group       | Subject analysis set | Subject analysis set  |
| Number of subjects analysed | 48                                   | 49                    | 96                   | 49                    |
| Units: participants         |                                      |                       |                      |                       |
| TEAEs                       | 33                                   | 31                    | 46                   | 26                    |
| TESAEs                      | 2                                    | 2                     | 1                    | 1                     |

|                             |                       |  |  |  |
|-----------------------------|-----------------------|--|--|--|
| <b>End point values</b>     | Mavrilimumab<br>100mg |  |  |  |
| Subject group type          | Subject analysis set  |  |  |  |
| Number of subjects analysed | 48                    |  |  |  |
| Units: participants         |                       |  |  |  |
| TEAEs                       | 28                    |  |  |  |
| TESAEs                      | 0                     |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants With Abnormal Vital Signs Reported as Treatment-Emergent Adverse Events (TEAEs)

|                 |  |
|-----------------|--|
| End point title | Number of Participants With Abnormal Vital Signs Reported as Treatment-Emergent Adverse Events (TEAEs) <sup>[55]</sup> <sup>[56]</sup> |
|-----------------|--|

End point description:

Vital sign assessments included blood pressure, pulse rate, temperature, and respiration rate. Vital signs abnormalities reported as TEAEs were reported. The safety population included all participants who received any dose of investigational product.

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

End point timeframe:

Baseline up to Day 169 (follow-up)

Notes:

[55] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

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

Justification: The subject analysis sets were created for the safety population due to difference in evaluable participants for the reporting groups and data has been represented accordingly; hence not all the baseline period arms included while reporting end point data.

|                             |                                      |                       |                      |                       |
|-----------------------------|--------------------------------------|-----------------------|----------------------|-----------------------|
| <b>End point values</b>     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Placebo              | Mavrilimumab<br>50 mg |
| Subject group type          | Reporting group                      | Reporting group       | Subject analysis set | Subject analysis set  |
| Number of subjects analysed | 48                                   | 49                    | 96                   | 49                    |
| Units: participants         |                                      |                       |                      |                       |
| Pyrexia                     | 0                                    | 0                     | 1                    | 2                     |
| Hypertension                | 0                                    | 1                     | 2                    | 0                     |

|                             |                       |  |  |  |
|-----------------------------|-----------------------|--|--|--|
| <b>End point values</b>     | Mavrilimumab<br>100mg |  |  |  |
| Subject group type          | Subject analysis set  |  |  |  |
| Number of subjects analysed | 48                    |  |  |  |

|                     |   |  |  |  |
|---------------------|---|--|--|--|
| Units: participants |   |  |  |  |
| Pyrexia             | 0 |  |  |  |
| Hypertension        | 0 |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants With Abnormal Electrocardiogram (ECG) Results

|                 |  |
|-----------------|--|
| End point title | Number of Participants With Abnormal Electrocardiogram (ECG) Results <sup>[57]</sup> <sup>[58]</sup> |
|-----------------|--|

End point description:

12-lead ECG was recorded and corrected QT (QTc) interval was measured with the participant in a rested supine position for at least 10 minutes. Any ECG abnormality deemed clinically significant as per investigator's discretion were reported. The safety population included all participants who received any dose of investigational product.

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

End point timeframe:

Baseline up to Day 169 (follow-up)

Notes:

[57] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

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

Justification: The subject analysis sets were created for the safety population due to difference in evaluable participants for the reporting groups and data has been represented accordingly; hence not all the baseline period arms included while reporting end point data.

| End point values            | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Placebo              | Mavrilimumab<br>50 mg |
|-----------------------------|--------------------------------------|-----------------------|----------------------|-----------------------|
| Subject group type          | Reporting group                      | Reporting group       | Subject analysis set | Subject analysis set  |
| Number of subjects analysed | 48                                   | 49                    | 96                   | 49                    |
| Units: participants         | 1                                    | 0                     | 0                    | 0                     |

| End point values            | Mavrilimumab<br>100mg |  |  |  |
|-----------------------------|-----------------------|--|--|--|
| Subject group type          | Subject analysis set  |  |  |  |
| Number of subjects analysed | 48                    |  |  |  |
| Units: participants         | 2                     |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Forced Expiratory Volume in 1 Second (FEV1) and Forced Vital Capacity

**(FVC) at Day 85**

|                 |   |
|-----------------|---|
| End point title | Forced Expiratory Volume in 1 Second (FEV1) and Forced Vital Capacity (FVC) at Day 85 <sup>[59]</sup> <sup>[60]</sup> |
|-----------------|---|

End point description:

FEV1 was the maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration. FVC was the volume of air which can be forcibly exhaled from the lungs after taking the deepest breath possible. The safety population included all participants who received any dose of investigational product. Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure.

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

End point timeframe:

Day 85

Notes:

[59] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

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

Justification: The subject analysis sets were created for the safety population due to difference in evaluable participants for the reporting groups and data has been represented accordingly; hence not all the baseline period arms included while reporting end point data.

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>100 mg | Placebo         |
|--------------------------------------|--------------------------------------|-----------------------|------------------------|-----------------|
| Subject group type                   | Reporting group                      | Reporting group       | Reporting group        | Reporting group |
| Number of subjects analysed          | 46                                   | 47                    | 47                     | 87              |
| Units: liters                        |                                      |                       |                        |                 |
| arithmetic mean (standard deviation) |                                      |                       |                        |                 |
| FEV1                                 | 2.877 (± 0.821)                      | 2.949 (± 0.722)       | 2.793 (± 0.69)         | 2.73 (± 0.764)  |
| FVC                                  | 3.582 (± 0.967)                      | 3.667 (± 0.882)       | 3.499 (± 0.766)        | 3.439 (± 0.949) |

| End point values                     | Mavrilimumab<br>50 mg |  |  |  |
|--------------------------------------|-----------------------|--|--|--|
| Subject group type                   | Subject analysis set  |  |  |  |
| Number of subjects analysed          | 49                    |  |  |  |
| Units: liters                        |                       |  |  |  |
| arithmetic mean (standard deviation) |                       |  |  |  |
| FEV1                                 | 2.701 (± 0.489)       |  |  |  |
| FVC                                  | 3.37 (± 0.527)        |  |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Primary: Forced Expiratory Volume in 1 Second (FEV1) and Forced Vital Capacity (FVC) at Day 85 by Region**

|                 |  |
|-----------------|--|
| End point title | Forced Expiratory Volume in 1 Second (FEV1) and Forced Vital |
|-----------------|--|

## End point description:

FEV1 was the maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration. FVC was the volume of air which can be forcibly exhaled from the lungs after taking the deepest breath possible. FEV1 and FVC at Day 85 for the European and Japanese regions were reported. The safety population included all participants who received any dose of investigational product. Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure and "n" signifies participants who were evaluable for the specified region for each arm, respectively.

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

End point timeframe:

Day 85

## Notes:

[61] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

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

Justification: The subject analysis sets were created for the safety population due to difference in evaluable participants for the reporting groups and data has been represented accordingly; hence not all the baseline period arms included while reporting end point data.

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>100 mg | Placebo         |
|--------------------------------------|--------------------------------------|-----------------------|------------------------|-----------------|
| Subject group type                   | Reporting group                      | Reporting group       | Reporting group        | Reporting group |
| Number of subjects analysed          | 46                                   | 47                    | 47                     | 87              |
| Units: liters                        |                                      |                       |                        |                 |
| arithmetic mean (standard deviation) |                                      |                       |                        |                 |
| European: FEV1 (n=71,37,39,40,39)    | 2.902 (± 0.81)                       | 3.042 (± 0.745)       | 2.848 (± 0.699)        | 2.811 (± 0.79)  |
| European: FVC (n=71,37,39,40,39)     | 3.632 (± 0.948)                      | 3.779 (± 0.917)       | 3.553 (± 0.772)        | 3.537 (± 0.996) |
| Japanese: FEV1 (n=16,9,8,9,8)        | 2.774 (± 0.908)                      | 2.493 (± 0.354)       | 2.52 (± 0.616)         | 2.367 (± 0.51)  |
| Japanese: FVC (n=16,9,8,9,8)         | 3.378 (± 1.076)                      | 3.119 (± 0.37)        | 3.235 (± 0.725)        | 3.005 (± 0.534) |

| End point values                     | Mavrilimumab<br>50 mg |  |  |  |
|--------------------------------------|-----------------------|--|--|--|
| Subject group type                   | Subject analysis set  |  |  |  |
| Number of subjects analysed          | 49                    |  |  |  |
| Units: liters                        |                       |  |  |  |
| arithmetic mean (standard deviation) |                       |  |  |  |
| European: FEV1 (n=71,37,39,40,39)    | 2.698 (± 0.501)       |  |  |  |
| European: FVC (n=71,37,39,40,39)     | 3.355 (± 0.537)       |  |  |  |
| Japanese: FEV1 (n=16,9,8,9,8)        | 2.712 (± 0.457)       |  |  |  |
| Japanese: FVC (n=16,9,8,9,8)         | 3.434 (± 0.505)       |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Change From Baseline in Forced Expiratory Volume in 1 Second (FEV1) and Forced Vital Capacity (FVC) at Day 85

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Forced Expiratory Volume in 1 Second (FEV1) and Forced Vital Capacity (FVC) at Day 85 <sup>[63]</sup> <sup>[64]</sup> |
|-----------------|---|

End point description:

FEV1 was the maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration. FVC was the volume of air which can be forcibly exhaled from the lungs after taking the deepest breath possible. The safety population included all participants who received any dose of investigational product. Here "n" signifies participants who were evaluable for this measure at the specified time point for each arm, respectively.

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

End point timeframe:

Baseline and Day 85

Notes:

[63] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

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

Justification: The subject analysis sets were created for the safety population due to difference in evaluable participants for the reporting groups and data has been represented accordingly; hence not all the baseline period arms included while reporting end point data.

| End point values                             | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Placebo              | Mavrilimumab<br>50 mg |
|--|--------------------------------------|-----------------------|----------------------|-----------------------|
| Subject group type                           | Reporting group                      | Reporting group       | Subject analysis set | Subject analysis set  |
| Number of subjects analysed                  | 48                                   | 49                    | 96                   | 49                    |
| Units: liters                                |                                      |                       |                      |                       |
| arithmetic mean (standard deviation)         |                                      |                       |                      |                       |
| Baseline: FEV1 (n=87,43,45,49,48)            | 2.788 (± 0.773)                      | 2.99 (± 0.765)        | 2.79 (± 0.77)        | 2.76 (± 0.43)         |
| Change at Day 85: FEV1<br>(n=87,46,47,49,47) | 0.044 (± 0.231)                      | 0.016 (± 0.196)       | -0.039 (± 0.234)     | -0.059 (± 0.249)      |
| Baseline: FVC (n=87,43,45,49,48)             | 3.486 (± 0.963)                      | 3.759 (± 0.868)       | 3.456 (± 0.948)      | 3.409 (± 0.496)       |
| Change at Day 85: FVC<br>(n=87,46,47,49,47)  | 0.048 (± 0.243)                      | -0.013 (± 0.239)      | -0.012 (± 0.301)     | -0.039 (± 0.496)      |

| End point values                             | Mavrilimumab<br>100mg |  |  |  |
|--|-----------------------|--|--|--|
| Subject group type                           | Subject analysis set  |  |  |  |
| Number of subjects analysed                  | 48                    |  |  |  |
| Units: liters                                |                       |  |  |  |
| arithmetic mean (standard deviation)         |                       |  |  |  |
| Baseline: FEV1 (n=87,43,45,49,48)            | 2.831 (± 0.681)       |  |  |  |
| Change at Day 85: FEV1<br>(n=87,46,47,49,47) | -0.049 (± 0.221)      |  |  |  |
| Baseline: FVC (n=87,43,45,49,48)             | 3.506 (± 0.804)       |  |  |  |



|   |                          |  |  |  |
|---|--------------------------|--|--|--|
| Change at Day 85: FVC<br>(n=87,46,47,49,47) | -0.017 ( $\pm$<br>0.218) |  |  |  |
|---|--------------------------|--|--|--|

## Statistical analyses

No statistical analyses for this end point

## Primary: Diffusing Capacity for Carbon Monoxide (DLCO) at Day 85

|                 |   |
|-----------------|---|
| End point title | Diffusing Capacity for Carbon Monoxide (DLCO) at Day 85 <sup>[65]</sup> <sup>[66]</sup> |
|-----------------|---|

End point description:

DLCO is a pulmonary function test that measures the partial pressure difference between inspired and expired carbon monoxide. The safety population included all participants who received any dose of investigational product. Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure.

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

End point timeframe:

Day 85

Notes:

[65] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

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

Justification: The subject analysis sets were created for the safety population due to difference in evaluable participants for the reporting groups and data has been represented accordingly; hence not all the baseline period arms included while reporting end point data.

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>100 mg | Placebo            |
|--------------------------------------|--------------------------------------|-----------------------|------------------------|--------------------|
| Subject group type                   | Reporting group                      | Reporting group       | Reporting group        | Reporting group    |
| Number of subjects analysed          | 46                                   | 47                    | 47                     | 87                 |
| Units: percent diffusion capacity    |                                      |                       |                        |                    |
| arithmetic mean (standard deviation) | 95 ( $\pm$ 16.2)                     | 95 ( $\pm$ 15.1)      | 89.3 ( $\pm$ 12)       | 91.7 ( $\pm$ 16.7) |

| End point values                     | Mavrilimumab<br>50 mg |  |  |  |
|--------------------------------------|-----------------------|--|--|--|
| Subject group type                   | Subject analysis set  |  |  |  |
| Number of subjects analysed          | 49                    |  |  |  |
| Units: percent diffusion capacity    |                       |  |  |  |
| arithmetic mean (standard deviation) | 95 ( $\pm$ 15.7)      |  |  |  |

## Statistical analyses

No statistical analyses for this end point

**Primary: Diffusing Capacity for Carbon Monoxide (DLCO) at Day 85 by Region**

|                 |   |
|-----------------|---|
| End point title | Diffusing Capacity for Carbon Monoxide (DLCO) at Day 85 by Region <sup>[67]</sup> <sup>[68]</sup> |
|-----------------|---|

End point description:

DLCO is a pulmonary function test, and measures the partial pressure difference between inspired and expired carbon monoxide. DLCO% for the European and Japanese regions were reported. The safety population included all participants who received any dose of investigational product. Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure and "n" signifies participants who were evaluable for this measure for the specified region for each arm, respectively.

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

End point timeframe:

Day 85

Notes:

[67] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

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

Justification: The subject analysis sets were created for the safety population due to difference in evaluable participants for the reporting groups and data has been represented accordingly; hence not all the baseline period arms included while reporting end point data.

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>100 mg | Placebo         |
|--------------------------------------|--------------------------------------|-----------------------|------------------------|-----------------|
| Subject group type                   | Reporting group                      | Reporting group       | Reporting group        | Reporting group |
| Number of subjects analysed          | 46                                   | 47                    | 47                     | 87              |
| Units: percent diffusion capacity    |                                      |                       |                        |                 |
| arithmetic mean (standard deviation) |                                      |                       |                        |                 |
| European region: (n=71,37,39,40,39)  | 96 (± 16.9)                          | 94 (± 15.2)           | 88.6 (± 10.7)          | 90.4 (± 16.5)   |
| Japanese region (n=16,9,8,9,8)       | 91 (± 13.3)                          | 100.1 (± 14.6)        | 93 (± 17.2)            | 97.6 (± 16.9)   |

| End point values                     | Mavrilimumab<br>50 mg |  |  |  |
|--------------------------------------|-----------------------|--|--|--|
| Subject group type                   | Subject analysis set  |  |  |  |
| Number of subjects analysed          | 49                    |  |  |  |
| Units: percent diffusion capacity    |                       |  |  |  |
| arithmetic mean (standard deviation) |                       |  |  |  |
| European region: (n=71,37,39,40,39)  | 94.8 (± 16.5)         |  |  |  |
| Japanese region (n=16,9,8,9,8)       | 96 (± 12.6)           |  |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Primary: Change from Baseline in Diffusing Capacity for Carbon Monoxide (DLCO) at Day 85**

|                 |   |
|-----------------|---|
| End point title | Change from Baseline in Diffusing Capacity for Carbon Monoxide (DLCO) at Day 85 <sup>[69]</sup> <sup>[70]</sup> |
|-----------------|---|

**End point description:**

DLCO is a pulmonary function test, and measures the partial pressure difference between inspired and expired carbon monoxide. The safety population included all participants who received any dose of investigational product. Here "n" signifies participants who were evaluable for this measure at the specified time point for each arm, respectively.

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

**End point timeframe:**

Baseline and Day 85

**Notes:**

[69] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

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

Justification: The subject analysis sets were created for the safety population due to difference in evaluable participants for the reporting groups and data has been represented accordingly; hence not all the baseline period arms included while reporting end point data.

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Placebo              | Mavrilimumab<br>50 mg |
|--------------------------------------|--------------------------------------|-----------------------|----------------------|-----------------------|
| Subject group type                   | Reporting group                      | Reporting group       | Subject analysis set | Subject analysis set  |
| Number of subjects analysed          | 48                                   | 49                    | 96                   | 49                    |
| Units: percent diffusion capacity    |                                      |                       |                      |                       |
| arithmetic mean (standard deviation) |                                      |                       |                      |                       |
| Baseline (n=86,40,45,49,48)          | 96.3 (± 17.7)                        | 93.7 (± 15.5)         | 91.5 (± 12.5)        | 97.5 (± 14.8)         |
| Change at Day 85 (n=87,46,47,49,47)  | -3.1 (± 17.3)                        | 0.4 (± 11.1)          | 0.1 (± 14.3)         | -2.5 (± 10.8)         |

| End point values                     | Mavrilimumab<br>100mg |  |  |  |
|--------------------------------------|-----------------------|--|--|--|
| Subject group type                   | Subject analysis set  |  |  |  |
| Number of subjects analysed          | 48                    |  |  |  |
| Units: percent diffusion capacity    |                       |  |  |  |
| arithmetic mean (standard deviation) |                       |  |  |  |
| Baseline (n=86,40,45,49,48)          | 92.5 (± 13.7)         |  |  |  |
| Change at Day 85 (n=87,46,47,49,47)  | -3.7 (± 11.3)         |  |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Primary: Dyspnea Score at Day 85**

|                 |   |
|-----------------|---|
| End point title | Dyspnea Score at Day 85 <sup>[71][72]</sup> |
|-----------------|---|

**End point description:**

Modified Borg dyspnea scale is a validated participant reported outcome assessing participant's perceived difficulty in breathing (dyspnea). The scale ranges from 0 (nothing at all) to 10 (maximal difficulty). Higher scores indicate greater difficulty in breathing. The safety population included all participants who received any dose of investigational product.

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

End point timeframe:

Day 85

Notes:

[71] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

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

Justification: The subject analysis sets were created for the safety population due to difference in evaluable participants for the reporting groups and data has been represented accordingly; hence not all the baseline period arms included while reporting end point data.

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>100 mg | Placebo         |
|--------------------------------------|--------------------------------------|-----------------------|------------------------|-----------------|
| Subject group type                   | Reporting group                      | Reporting group       | Reporting group        | Reporting group |
| Number of subjects analysed          | 45                                   | 47                    | 47                     | 89              |
| Units: units on a scale              |                                      |                       |                        |                 |
| arithmetic mean (standard deviation) | 0.13 (± 0.38)                        | 0.35 (± 0.7)          | 0.35 (± 0.59)          | 0.25 (± 0.48)   |

| End point values                     | Mavrilimumab<br>50 mg |  |  |  |
|--------------------------------------|-----------------------|--|--|--|
| Subject group type                   | Subject analysis set  |  |  |  |
| Number of subjects analysed          | 49                    |  |  |  |
| Units: units on a scale              |                       |  |  |  |
| arithmetic mean (standard deviation) | 0.15 (± 0.44)         |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Change from Baseline in Dyspnea Score at Day 85

|                 |   |
|-----------------|---|
| End point title | Change from Baseline in Dyspnea Score at Day 85 <sup>[73]</sup> <sup>[74]</sup> |
|-----------------|---|

End point description:

Modified Borg dyspnea scale is a validated participant reported outcome assessing participant's perceived difficulty in breathing (dyspnea). The scale ranges from 0 (nothing at all) to 10 (maximal difficulty). Higher scores indicate greater difficulty in breathing. The safety population included all participants who received any dose of investigational product. Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure.

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

End point timeframe:

Baseline and Day 85

Notes:

[73] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

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

Justification: The subject analysis sets were created for the safety population due to difference in evaluable participants for the reporting groups and data has been represented accordingly; hence not all

the baseline period arms included while reporting end point data.

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Placebo              | Mavrilimumab<br>50 mg |
|--------------------------------------|--------------------------------------|-----------------------|----------------------|-----------------------|
| Subject group type                   | Reporting group                      | Reporting group       | Subject analysis set | Subject analysis set  |
| Number of subjects analysed          | 48                                   | 49                    | 96                   | 49                    |
| Units: units on a scale              |                                      |                       |                      |                       |
| arithmetic mean (standard deviation) |                                      |                       |                      |                       |
| Baseline (n=96,48,49,49,48)          | 0.26 (± 0.88)                        | 0.26 (± 0.59)         | 0.29 (± 0.58)        | 0.19 (± 0.49)         |
| Change at Day 85 (n=89,45,47,49,47)  | -0.14 (± 0.62)                       | 0.1 (± 0.44)          | -0.06 (± 0.53)       | -0.04 (± 0.35)        |

| End point values                     | Mavrilimumab<br>100mg |  |  |  |
|--------------------------------------|-----------------------|--|--|--|
| Subject group type                   | Subject analysis set  |  |  |  |
| Number of subjects analysed          | 48                    |  |  |  |
| Units: units on a scale              |                       |  |  |  |
| arithmetic mean (standard deviation) |                       |  |  |  |
| Baseline (n=96,48,49,49,48)          | 0.32 (± 0.59)         |  |  |  |
| Change at Day 85 (n=89,45,47,49,47)  | 0.02 (± 0.56)         |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Categorized Dyspnea Score at Day 85

|   |   |
|---|---|
| End point title   | Categorized Dyspnea Score at Day 85 <sup>[75]</sup> <sup>[76]</sup> |
| End point description:  |   |
| Modified Borg dyspnea scale is a validated participant reported outcome assessing participant's perceived difficulty in breathing (dyspnea). The scale ranges from 0 (nothing at all) to 10 (maximal difficulty). Higher scores indicate greater difficulty in breathing. The modified BORG dyspnea scale was categorized as - no/slight (0 to 2), moderate (3 and 4), severe (5 and 6) and very severe breathlessness (7 and above). The safety population included all participants who received any dose of investigational product. Here "n" signifies participants who were evaluable for this measure at the specified time point for each arm, respectively. |   |
| End point type  | Primary   |
| End point timeframe:  |   |
| Day 85  |   |

Notes:

[75] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

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

Justification: The subject analysis sets were created for the safety population due to difference in evaluable participants for the reporting groups and data has been represented accordingly; hence not all the baseline period arms included while reporting end point data.

| End point values            | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>100 mg | Placebo         |
|-----------------------------|--------------------------------------|-----------------------|------------------------|-----------------|
| Subject group type          | Reporting group                      | Reporting group       | Reporting group        | Reporting group |
| Number of subjects analysed | 45                                   | 47                    | 47                     | 89              |
| Units: participants         |                                      |                       |                        |                 |
| No/Slight breathlessness    | 45                                   | 45                    | 46                     | 89              |
| Moderate breathlessness     | 0                                    | 2                     | 1                      | 0               |
| Severe breathlessness       | 0                                    | 0                     | 0                      | 0               |
| Very severe breathlessness  | 0                                    | 0                     | 0                      | 0               |

| End point values            | Mavrilimumab<br>50 mg |  |  |  |
|-----------------------------|-----------------------|--|--|--|
| Subject group type          | Subject analysis set  |  |  |  |
| Number of subjects analysed | 49                    |  |  |  |
| Units: participants         |                       |  |  |  |
| No/Slight breathlessness    | 49                    |  |  |  |
| Moderate breathlessness     | 0                     |  |  |  |
| Severe breathlessness       | 0                     |  |  |  |
| Very severe breathlessness  | 0                     |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Oxygen Saturation Level at Day 85

|                 |   |
|-----------------|---|
| End point title | Oxygen Saturation Level at Day 85 <sup>[77]</sup> <sup>[78]</sup> |
|-----------------|---|

End point description:

Oxygen saturation measured by pulse oximetry which measures the concentration of oxygen in the blood. The safety population included all participants who received any dose of investigational product. Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure.

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

End point timeframe:

Day 85

Notes:

[77] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

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

Justification: The subject analysis sets were created for the safety population due to difference in evaluable participants for the reporting groups and data has been represented accordingly; hence not all the baseline period arms included while reporting end point data.

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>100 mg | Placebo         |
|--------------------------------------|--------------------------------------|-----------------------|------------------------|-----------------|
| Subject group type                   | Reporting group                      | Reporting group       | Reporting group        | Reporting group |
| Number of subjects analysed          | 45                                   | 47                    | 47                     | 88              |
| Units: percent saturation            |                                      |                       |                        |                 |
| arithmetic mean (standard deviation) | 97.6 (± 1.3)                         | 97.7 (± 1.3)          | 97.3 (± 1.5)           | 97.5 (± 1.2)    |

| End point values                     | Mavrilimumab<br>50 mg |  |  |  |
|--------------------------------------|-----------------------|--|--|--|
| Subject group type                   | Subject analysis set  |  |  |  |
| Number of subjects analysed          | 49                    |  |  |  |
| Units: percent saturation            |                       |  |  |  |
| arithmetic mean (standard deviation) | 97.2 (± 1.8)          |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Oxygen Saturation Level at Day 85 by Region

|                 |   |
|-----------------|---|
| End point title | Oxygen Saturation Level at Day 85 by Region <sup>[79]</sup> <sup>[80]</sup> |
|-----------------|---|

End point description:

Oxygen saturation measured by pulse oximetry which measures the concentration of oxygen in the blood. Oxygen saturation for the European and Japanese regions were reported. The safety population included all participants who received any dose of investigational product. Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure and "n" signifies participants who were evaluable for this measure for the specified region for each arm, respectively.

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

End point timeframe:

Day 85

Notes:

[79] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

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

Justification: The subject analysis sets were created for the safety population due to difference in evaluable participants for the reporting groups and data has been represented accordingly; hence not all the baseline period arms included while reporting end point data.

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>100 mg | Placebo         |
|--------------------------------------|--------------------------------------|-----------------------|------------------------|-----------------|
| Subject group type                   | Reporting group                      | Reporting group       | Reporting group        | Reporting group |
| Number of subjects analysed          | 45                                   | 47                    | 47                     | 88              |
| Units: percent saturation            |                                      |                       |                        |                 |
| arithmetic mean (standard deviation) |                                      |                       |                        |                 |
| European region: (n=72,36,39,40,39)  | 97.6 (± 1.3)                         | 97.6 (± 1.3)          | 97.3 (± 1.6)           | 97.5 (± 1.3)    |
| Japanese region: (n=16,9,8,9,8)      | 97.4 (± 1)                           | 98.4 (± 1.1)          | 97.3 (± 1.3)           | 97.6 (± 0.9)    |

|  |                            |  |  |  |
|--|----------------------------|--|--|--|
| <b>End point values</b>  | Mavrilimumab<br>50 mg      |  |  |  |
| Subject group type   | Subject analysis set       |  |  |  |
| Number of subjects analysed  | 49                         |  |  |  |
| Units: percent saturation  |                            |  |  |  |
| arithmetic mean (standard deviation)                                   |                            |  |  |  |
| European region: (n=72,36,39,40,39)<br>Japanese region: (n=16,9,8,9,8) | 97.2 (± 2)<br>97.4 (± 0.7) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Change from Baseline in Oxygen Saturation Level at Day 85

|                 |  |
|-----------------|--|
| End point title | Change from Baseline in Oxygen Saturation Level at Day |
|-----------------|--|

End point description:

Oxygen saturation measured by pulse oximetry which measures the concentration of oxygen in the blood. The safety population included all participants who received any dose of investigational product. Here "n" signifies participants who were evaluable for this measure at the specified time point for each arm, respectively.

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

End point timeframe:

Baseline and Day 85

Notes:

[81] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

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

Justification: The subject analysis sets were created for the safety population due to difference in evaluable participants for the reporting groups and data has been represented accordingly; hence not all the baseline period arms included while reporting end point data.

|                                      |                                      |                       |                      |                       |
|--------------------------------------|--------------------------------------|-----------------------|----------------------|-----------------------|
| <b>End point values</b>              | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Placebo              | Mavrilimumab<br>50 mg |
| Subject group type                   | Reporting group                      | Reporting group       | Subject analysis set | Subject analysis set  |
| Number of subjects analysed          | 48                                   | 49                    | 96                   | 49                    |
| Units: percent saturation            |                                      |                       |                      |                       |
| arithmetic mean (standard deviation) |                                      |                       |                      |                       |
| Baseline (n=96,48,49,49,48)          | 97.8 (± 1.6)                         | 97.6 (± 1.2)          | 97.5 (± 1.3)         | 97.6 (± 1.4)          |
| Change at Day 85 (n=88,45,47,49,47)  | -0.2 (± 1.5)                         | 0.1 (± 1.4)           | 0 (± 1.5)            | -0.3 (± 1.9)          |

|                         |                       |  |  |  |
|-------------------------|-----------------------|--|--|--|
| <b>End point values</b> | Mavrilimumab<br>100mg |  |  |  |
|-------------------------|-----------------------|--|--|--|



|                                      |                      |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| Subject group type                   | Subject analysis set |  |  |  |
| Number of subjects analysed          | 48                   |  |  |  |
| Units: percent saturation            |                      |  |  |  |
| arithmetic mean (standard deviation) |                      |  |  |  |
| Baseline (n=96,48,49,49,48)          | 97.2 (± 1.7)         |  |  |  |
| Change at Day 85 (n=88,45,47,49,47)  | 0.1 (± 2.1)          |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of Participants with Abnormal Clinical Laboratory Parameters Reported as Treatment-Emergent Adverse Events (TEAEs)

|                 |   |
|-----------------|---|
| End point title | Number of Participants with Abnormal Clinical Laboratory Parameters Reported as Treatment-Emergent Adverse Events (TEAEs) <sup>[83][84]</sup> |
|-----------------|---|

End point description:

Any medically significant change in laboratory evaluations were recorded as adverse events. Following parameters were analyzed for laboratory examination: hematology (haemoglobin, reticulocytes, platelet count, white blood cell count, total neutrophils, eosinophils, monocytes, basophils, lymphocytes, mean corpuscular volume, mean corpuscular haemoglobin concentration); serum chemistry (creatinine, glucose, calcium, sodium, potassium, chloride, total bicarbonate, aspartate aminotransferase, alanine aminotransferase, total bilirubin, alkaline phosphatase, gamma glutamyl transferase, CRP, ESR, albumin, total cholesterol, triglycerides, rheumatoid factor and anti-cyclic citrullinated peptide antibodies); urinalysis (albumin, glucose, protein, blood, nitrite). The safety population included all participants who received any dose of investigational product.

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

End point timeframe:

Baseline up to Day 169 (follow-up)

Notes:

[83] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

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

Justification: The subject analysis sets were created for the safety population due to difference in evaluable participants for the reporting groups and data has been represented accordingly; hence not all the baseline period arms included while reporting end point data.

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Placebo              | Mavrilimumab<br>50 mg |
|--------------------------------------|--------------------------------------|-----------------------|----------------------|-----------------------|
| Subject group type                   | Reporting group                      | Reporting group       | Subject analysis set | Subject analysis set  |
| Number of subjects analysed          | 48                                   | 49                    | 96                   | 49                    |
| Units: participants                  |                                      |                       |                      |                       |
| Blood and lymphatic system disorders | 3                                    | 3                     | 10                   | 3                     |
| Hepatic abnormality                  | 5                                    | 3                     | 3                    | 2                     |
| Blood cholesterol increased          | 0                                    | 0                     | 0                    | 1                     |
| Blood triglycerides increased        | 0                                    | 0                     | 1                    | 0                     |
| Hypercholesterolemia                 | 1                                    | 1                     | 1                    | 1                     |
| Hyperglycemia                        | 0                                    | 0                     | 1                    | 1                     |
| Urinalysis abnormalities             | 0                                    | 3                     | 3                    | 1                     |

|                                      |                      |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| <b>End point values</b>              | Mavrimumab<br>100mg  |  |  |  |
| Subject group type                   | Subject analysis set |  |  |  |
| Number of subjects analysed          | 48                   |  |  |  |
| Units: participants                  |                      |  |  |  |
| Blood and lymphatic system disorders | 4                    |  |  |  |
| Hepatic abnormality                  | 3                    |  |  |  |
| Blood cholesterol increased          | 0                    |  |  |  |
| Blood triglycerides increased        | 0                    |  |  |  |
| Hypercholesterolemia                 | 0                    |  |  |  |
| Hyperglycemia                        | 0                    |  |  |  |
| Urinalysis abnormalities             | 0                    |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in DAS28 (CRP) and DAS28 (ESR) at Day 85

|                 |   |
|-----------------|---|
| End point title | Change from Baseline in DAS28 (CRP) and DAS28 (ESR) at Day 85 |
|-----------------|---|

End point description:

DAS28 calculated SJC and TJC using the 28 joints, GH using participant assessment of disease activity (participant rated arthritis activity using the numerical rating scale with 0 = best, 10 = worst) and CRP (mg/L) for DAS28 (CRP) or ESR (mm/hour) for DAS28 (ESR). Total score range: 0-9.4, higher score = more disease activity. DAS28 <3.2 = low disease activity, >=3.2 to 5.1 = moderate to high disease activity and <2.6= remission. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues. Here "n" signifies participants who were evaluable for this measure for the specified time point for each arm, respectively.

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

End point timeframe:

Baseline and Day 85

|  |                                    |                     |                     |                      |
|--|------------------------------------|---------------------|---------------------|----------------------|
| <b>End point values</b>                            | Mavrimumab<br>10 milligram<br>(mg) | Mavrimumab<br>30 mg | Mavrimumab<br>50 mg | Mavrimumab<br>100 mg |
| Subject group type                                 | Reporting group                    | Reporting group     | Reporting group     | Reporting group      |
| Number of subjects analysed                        | 48                                 | 49                  | 48                  | 47                   |
| Units: units on a scale                            |                                    |                     |                     |                      |
| arithmetic mean (standard error)                   |                                    |                     |                     |                      |
| DAS28(CRP): Baseline<br>(n=92,48,49,48,47)         | 5.24 (± 0.16)                      | 5.42 (± 0.139)      | 5.14 (± 0.146)      | 5.34 (± 0.115)       |
| DAS28(CRP): Change at Day 85<br>(n=84,45,46,48,46) | -1.27 (± 0.166)                    | -1.63 (± 0.163)     | -1.32 (± 0.162)     | -1.7 (± 0.165)       |
| DAS28(ESR): Baseline:<br>(n=92,48,49,48,47)        | 6.06 (± 0.165)                     | 6.31 (± 0.145)      | 5.98 (± 0.163)      | 6.06 (± 0.119)       |

|  |                      |                    |                      |                      |
|--|----------------------|--------------------|----------------------|----------------------|
| DAS28(ESR): Change at Day 85<br>(n=85,45,47,48,46) | -1.39 ( $\pm$ 0.172) | -1.8 ( $\pm$ 0.17) | -1.46 ( $\pm$ 0.168) | -1.84 ( $\pm$ 0.172) |
|--|----------------------|--------------------|----------------------|----------------------|

| End point values                                   | Placebo              |  |  |  |
|--|----------------------|--|--|--|
| Subject group type                                 | Reporting group      |  |  |  |
| Number of subjects analysed                        | 92                   |  |  |  |
| Units: units on a scale                            |                      |  |  |  |
| arithmetic mean (standard error)                   |                      |  |  |  |
| DAS28(CRP): Baseline<br>(n=92,48,49,48,47)         | 5.43 ( $\pm$ 0.11)   |  |  |  |
| DAS28(CRP): Change at Day 85<br>(n=84,45,46,48,46) | -0.97 ( $\pm$ 0.12)  |  |  |  |
| DAS28(ESR): Baseline:<br>(n=92,48,49,48,47)        | 6.18 ( $\pm$ 0.118)  |  |  |  |
| DAS28(ESR): Change at Day 85<br>(n=85,45,47,48,46) | -1.04 ( $\pm$ 0.125) |  |  |  |

## Statistical analyses

| Statistical analysis title   | Statistical Analysis 1                   |
|--|--|
| Statistical analysis description:  |  |
| Analysis reported for change from baseline in DAS28 (CRP) at Day 85. Analysis Type used was dose escalation. |  |
| Comparison groups  | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis  | 140                                      |
| Analysis specification   | Pre-specified                            |
| Analysis type  | other <sup>[85]</sup>                    |
| P-value  | = 0.137                                  |
| Method   | Repeated measures model                  |
| Parameter estimate   | Adjusted mean difference                 |
| Point estimate   | -0.31                                    |
| Confidence interval  |  |
| level  | 95 %                                     |
| sides  | 2-sided                                  |
| lower limit  | -0.71                                    |
| upper limit  | 0.1                                      |
| Variability estimate   | Standard error of the mean               |
| Dispersion value   | 0.205                                    |

Notes:

[85] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

| Statistical analysis title   | Statistical Analysis 2       |
|--|------------------------------|
| Statistical analysis description:  |                              |
| Analysis reported for change from baseline in DAS28 (CRP) at Day 85. Analysis Type used was dose escalation. |                              |
| Comparison groups  | Placebo v Mavrilimumab 30 mg |

|   |                            |
|---|----------------------------|
| Number of subjects included in analysis | 141                        |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other <sup>[86]</sup>      |
| P-value                                 | = 0.001                    |
| Method                                  | Repeated measures model    |
| Parameter estimate                      | Adjusted mean difference   |
| Point estimate                          | -0.67                      |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | -1.07                      |
| upper limit                             | -0.27                      |
| Variability estimate                    | Standard error of the mean |
| Dispersion value                        | 0.202                      |

Notes:

[86] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis reported for change from baseline in DAS28 (CRP) at Day 85. Analysis Type used was dose escalation.

|   |                              |
|---|------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 140                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[87]</sup>        |
| P-value                                 | = 0.08                       |
| Method                                  | Repeated measures model      |
| Parameter estimate                      | Adjusted mean difference     |
| Point estimate                          | -0.35                        |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -0.75                        |
| upper limit                             | 0.04                         |
| Variability estimate                    | Standard error of the mean   |
| Dispersion value                        | 0.201                        |

Notes:

[87] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis reported for change from baseline in DAS28 (CRP) at Day 85. Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 139                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[88]</sup>         |
| P-value                                 | < 0.001                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted mean difference      |
| Point estimate                          | -0.74                         |

|                      |                            |
|----------------------|----------------------------|
| Confidence interval  |                            |
| level                | 95 %                       |
| sides                | 2-sided                    |
| lower limit          | -1.14                      |
| upper limit          | -0.33                      |
| Variability estimate | Standard error of the mean |
| Dispersion value     | 0.204                      |

Notes:

[88] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 5 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis reported for change from baseline in DAS28 (ESR) at Day 85. Analysis Type used was dose escalation.

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 140                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[89]</sup>                    |
| P-value                                 | = 0.107                                  |
| Method                                  | Repeated measures model                  |
| Parameter estimate                      | Adjusted mean difference                 |
| Point estimate                          | -0.34                                    |

Confidence interval

|                      |                            |
|----------------------|----------------------------|
| level                | 95 %                       |
| sides                | 2-sided                    |
| lower limit          | -0.76                      |
| upper limit          | 0.08                       |
| Variability estimate | Standard error of the mean |
| Dispersion value     | 0.212                      |

Notes:

[89] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 6 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis reported for change from baseline in DAS28 (ESR) at Day 85. Analysis Type used was dose escalation.

|   |                              |
|---|------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 141                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[90]</sup>        |
| P-value                                 | < 0.001                      |
| Method                                  | Repeated measures model      |
| Parameter estimate                      | Adjusted mean difference     |
| Point estimate                          | -0.76                        |

Confidence interval

|                      |                            |
|----------------------|----------------------------|
| level                | 95 %                       |
| sides                | 2-sided                    |
| lower limit          | -1.17                      |
| upper limit          | -0.35                      |
| Variability estimate | Standard error of the mean |
| Dispersion value     | 0.21                       |

Notes:

[90] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|  |                              |
|--|------------------------------|
| <b>Statistical analysis title</b>  | Statistical Analysis 7       |
| Statistical analysis description:  |                              |
| Analysis reported for change from baseline in DAS28 (ESR) at Day 85. Analysis Type used was dose escalation. |                              |
| Comparison groups  | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis  | 140                          |
| Analysis specification   | Pre-specified                |
| Analysis type  | other <sup>[91]</sup>        |
| P-value  | = 0.046                      |
| Method   | Repeated measures model      |
| Parameter estimate   | Adjusted mean difference     |
| Point estimate   | -0.42                        |
| Confidence interval  |                              |
| level  | 95 %                         |
| sides  | 2-sided                      |
| lower limit  | -0.83                        |
| upper limit  | -0.01                        |
| Variability estimate   | Standard error of the mean   |
| Dispersion value   | 0.209                        |

Notes:

[91] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|  |                               |
|--|-------------------------------|
| <b>Statistical analysis title</b>  | Statistical Analysis 8        |
| Statistical analysis description:  |                               |
| Analysis reported for change from baseline in DAS28 (ESR) at Day 85. Analysis Type used was dose escalation. |                               |
| Comparison groups  | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis  | 139                           |
| Analysis specification   | Pre-specified                 |
| Analysis type  | other <sup>[92]</sup>         |
| P-value  | < 0.001                       |
| Method   | Repeated measures model       |
| Parameter estimate   | Adjusted mean difference      |
| Point estimate   | -0.8                          |
| Confidence interval  |                               |
| level  | 95 %                          |
| sides  | 2-sided                       |
| lower limit  | -1.22                         |
| upper limit  | -0.38                         |
| Variability estimate   | Standard error of the mean    |
| Dispersion value   | 0.212                         |

Notes:

[92] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

## **Secondary: Change from Baseline in DAS28 (CRP) and DAS28 (ESR) at Day 85 by Region**

|                 |   |
|-----------------|---|
| End point title | Change from Baseline in DAS28 (CRP) and DAS28 (ESR) at Day 85 by Region |
|-----------------|---|

End point description:

DAS28 calculated SJC and TJC using the 28 joints, GH using participant assessment of disease activity (participant rated arthritis activity using the numerical rating scale with 0 = best, 10 = worst) and CRP (mg/L) for DAS28 (CRP) or ESR (mm/hour) for DAS28 (ESR). Total score range: 0-9.4, higher score = more disease activity. DAS28 <3.2 = low disease activity, >=3.2 to 5.1 = moderate to high disease activity and <2.6= remission. DAS28 (CRP) and DAS28 (ESR) for the European and Japanese regions were reported. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues. Here "n" signifies participants who were evaluable for this measure for the specified region for each arm, respectively.

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

End point timeframe:

Baseline and Day 85

| End point values                                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|--|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                                   | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed                          | 48                                   | 49                    | 48                    | 47                     |
| Units: units on a scale                              |                                      |                       |                       |                        |
| arithmetic mean (standard error)                     |                                      |                       |                       |                        |
| European: DAS28(CRP): Baseline<br>(n=75,39,41,39,39) | 5.3 (± 0.172)                        | 5.48 (± 0.154)        | 5.33 (± 0.155)        | 5.41 (± 0.111)         |
| European: DAS28(CRP): Day 85<br>(n=68,36,38,39,38)   | -1.4 (± 0.187)                       | -1.55 (± 0.181)       | -1.43 (± 0.181)       | -1.7 (± 0.183)         |
| Japanese: DAS28(CRP): Baseline<br>(n=17,9,8,9,8)     | 5 (± 0.427)                          | 5.12 (± 0.306)        | 4.32 (± 0.268)        | 5.04 (± 0.413)         |
| Japanese: DAS28(CRP): Day 85<br>(n=16,9,8,9,8)       | -0.73 (± 0.358)                      | -2.04 (± 0.381)       | -0.89 (± 0.361)       | -1.71 (± 0.38)         |
| European: DAS28(ESR): Baseline<br>(n=75,39,41,39,39) | 6.1 (± 0.18)                         | 6.36 (± 0.163)        | 6.23 (± 0.159)        | 6.12 (± 0.118)         |
| European: DAS28(ESR): Day 85<br>(n=69,36,39,39,38)   | -1.51 (± 0.196)                      | -1.76 (± 0.19)        | -1.53 (± 0.19)        | -1.85 (± 0.193)        |
| Japanese: DAS28(ESR): Baseline<br>(n=17,9,8,9,8)     | 5.87 (± 0.426)                       | 6.05 (± 0.309)        | 4.93 (± 0.379)        | 5.78 (± 0.404)         |
| Japanese: DAS28(ESR): Day 85<br>(n=16,9,8,9,8)       | -0.83 (± 0.359)                      | -1.99 (± 0.382)       | -1.24 (± 0.362)       | -1.78 (± 0.38)         |

| End point values                                     | Placebo         |  |  |  |
|--|-----------------|--|--|--|
| Subject group type                                   | Reporting group |  |  |  |
| Number of subjects analysed                          | 92              |  |  |  |
| Units: units on a scale                              |                 |  |  |  |
| arithmetic mean (standard error)                     |                 |  |  |  |
| European: DAS28(CRP): Baseline<br>(n=75,39,41,39,39) | 5.58 (± 0.117)  |  |  |  |
| European: DAS28(CRP): Day 85<br>(n=68,36,38,39,38)   | -1 (± 0.133)    |  |  |  |
| Japanese: DAS28(CRP): Baseline<br>(n=17,9,8,9,8)     | 4.75 (± 0.242)  |  |  |  |
| Japanese: DAS28(CRP): Day 85<br>(n=16,9,8,9,8)       | -0.85 (± 0.281) |  |  |  |
| European: DAS28(ESR): Baseline<br>(n=75,39,41,39,39) | 6.36 (± 0.124)  |  |  |  |

|  |                      |  |  |  |
|--|----------------------|--|--|--|
| European: DAS28(ESR): Day 85<br>(n=69,36,39,39,38) | -1.12 ( $\pm$ 0.14)  |  |  |  |
| Japanese: DAS28(ESR): Baseline<br>(n=17,9,8,9,8)   | 5.38 ( $\pm$ 0.248)  |  |  |  |
| Japanese: DAS28(ESR): Day 85<br>(n=16,9,8,9,8)     | -0.74 ( $\pm$ 0.276) |  |  |  |

## Statistical analyses

| Statistical analysis title  | Statistical Analysis 1                   |
|---|--|
| Statistical analysis description:   |  |
| European region: Analysis reported for change from baseline in DAS28 (CRP) at Day 85. Analysis Type used was dose escalation. |  |
| Comparison groups   | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis   | 140                                      |
| Analysis specification  | Pre-specified                            |
| Analysis type   | other <sup>[93]</sup>                    |
| P-value   | = 0.086                                  |
| Method  | Repeated measures model                  |
| Parameter estimate  | Adjusted mean difference                 |
| Point estimate  | -0.4                                     |
| Confidence interval   |  |
| level   | 95 %                                     |
| sides   | 2-sided                                  |
| lower limit   | -0.85                                    |
| upper limit   | 0.06                                     |
| Variability estimate  | Standard error of the mean               |
| Dispersion value  | 0.23                                     |

Notes:

[93] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

| Statistical analysis title  | Statistical Analysis 2       |
|---|------------------------------|
| Statistical analysis description:   |                              |
| European region: Analysis reported for change from baseline in DAS28 (CRP) at Day 85. Analysis Type used was dose escalation. |                              |
| Comparison groups   | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis   | 141                          |
| Analysis specification  | Pre-specified                |
| Analysis type   | other <sup>[94]</sup>        |
| P-value   | = 0.016                      |
| Method  | Repeated measures model      |
| Parameter estimate  | Adjusted mean difference     |
| Point estimate  | -0.55                        |
| Confidence interval   |                              |
| level   | 95 %                         |
| sides   | 2-sided                      |
| lower limit   | -0.99                        |
| upper limit   | -0.1                         |
| Variability estimate  | Standard error of the mean   |
| Dispersion value  | 0.225                        |



Notes:

[94] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>   | Statistical Analysis 3       |
| Statistical analysis description:   |                              |
| European region: Analysis reported for change from baseline in DAS28 (CRP) at Day 85. Analysis Type used was dose escalation. |                              |
| Comparison groups   | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis   | 140                          |
| Analysis specification  | Pre-specified                |
| Analysis type   | other <sup>[95]</sup>        |
| P-value   | = 0.059                      |
| Method  | Repeated measures model      |
| Parameter estimate  | Adjusted mean difference     |
| Point estimate  | -0.43                        |
| Confidence interval   |                              |
| level   | 95 %                         |
| sides   | 2-sided                      |
| lower limit   | -0.87                        |
| upper limit   | 0.02                         |
| Variability estimate  | Standard error of the mean   |
| Dispersion value  | 0.225                        |

Notes:

[95] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|   |                               |
|---|-------------------------------|
| <b>Statistical analysis title</b>   | Statistical Analysis 4        |
| Statistical analysis description:   |                               |
| European region: Analysis reported for change from baseline in DAS28 (CRP) at Day 85. Analysis Type used was dose escalation. |                               |
| Comparison groups   | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis   | 139                           |
| Analysis specification  | Pre-specified                 |
| Analysis type   | other <sup>[96]</sup>         |
| P-value   | = 0.002                       |
| Method  | Repeated measures model       |
| Parameter estimate  | Adjusted mean difference      |
| Point estimate  | -0.7                          |
| Confidence interval   |                               |
| level   | 95 %                          |
| sides   | 2-sided                       |
| lower limit   | -1.14                         |
| upper limit   | -0.25                         |
| Variability estimate  | Standard error of the mean    |
| Dispersion value  | 0.227                         |

Notes:

[96] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|   |                        |
|---|------------------------|
| <b>Statistical analysis title</b>   | Statistical Analysis 5 |
| Statistical analysis description:   |                        |
| European region: Analysis reported for change from baseline in DAS28 (ESR) at Day 85. Analysis Type used was dose escalation. |                        |

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 140                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[97]</sup>                    |
| P-value                                 | = 0.107                                  |
| Method                                  | Repeated measures model                  |
| Parameter estimate                      | Adjusted mean difference                 |
| Point estimate                          | -0.39                                    |
| Confidence interval                     |  |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | -0.87                                    |
| upper limit                             | 0.09                                     |
| Variability estimate                    | Standard error of the mean               |
| Dispersion value                        | 0.241                                    |

Notes:

[97] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>   | Statistical Analysis 6       |
| Statistical analysis description:   |                              |
| European region: Analysis reported for change from baseline in DAS28 (ESR) at Day 85. Analysis Type used was dose escalation. |                              |
| Comparison groups   | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis   | 141                          |
| Analysis specification  | Pre-specified                |
| Analysis type   | other <sup>[98]</sup>        |
| P-value   | = 0.007                      |
| Method  | Repeated measures model      |
| Parameter estimate  | Adjusted mean difference     |
| Point estimate  | -0.64                        |
| Confidence interval   |                              |
| level   | 95 %                         |
| sides   | 2-sided                      |
| lower limit   | -1.11                        |
| upper limit   | -0.18                        |
| Variability estimate  | Standard error of the mean   |
| Dispersion value  | 0.236                        |

Notes:

[98] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>   | Statistical Analysis 7       |
| Statistical analysis description:   |                              |
| European region: Analysis reported for change from baseline in DAS28 (ESR) at Day 85. Analysis Type used was dose escalation. |                              |
| Comparison groups   | Placebo v Mavrilimumab 50 mg |

|   |                            |
|---|----------------------------|
| Number of subjects included in analysis | 140                        |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other <sup>[99]</sup>      |
| P-value                                 | = 0.084                    |
| Method                                  | Repeated measures model    |
| Parameter estimate                      | Adjusted mean difference   |
| Point estimate                          | -0.41                      |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | -0.88                      |
| upper limit                             | 0.06                       |
| Variability estimate                    | Standard error of the mean |
| Dispersion value                        | 0.236                      |

Notes:

[99] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 8 |
|-----------------------------------|------------------------|

Statistical analysis description:

European region: Analysis reported for change from baseline in DAS28 (ESR) at Day 85. Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 139                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[100]</sup>        |
| P-value                                 | = 0.002                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted mean difference      |
| Point estimate                          | -0.73                         |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -1.2                          |
| upper limit                             | -0.26                         |
| Variability estimate                    | Standard error of the mean    |
| Dispersion value                        | 0.238                         |

Notes:

[100] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 9 |
|-----------------------------------|------------------------|

Statistical analysis description:

Japanese region: Analysis reported for change from baseline in DAS28 (CRP) at Day 85. Analysis Type used was dose escalation.

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 140                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[101]</sup>                   |
| P-value                                 | = 0.785                                  |
| Method                                  | Repeated measures model                  |
| Parameter estimate                      | Adjusted mean difference                 |
| Point estimate                          | 0.12                                     |

|                      |                            |
|----------------------|----------------------------|
| Confidence interval  |                            |
| level                | 95 %                       |
| sides                | 2-sided                    |
| lower limit          | -0.78                      |
| upper limit          | 1.02                       |
| Variability estimate | Standard error of the mean |
| Dispersion value     | 0.447                      |

Notes:

[101] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                         |
|-----------------------------------|-------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 10 |
|-----------------------------------|-------------------------|

Statistical analysis description:

Japanese region: Analysis reported for change from baseline in DAS28 (CRP) at Day 85. Analysis Type used was dose escalation.

|   |                              |
|---|------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 141                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[102]</sup>       |
| P-value                                 | = 0.014                      |
| Method                                  | Repeated measures model      |
| Parameter estimate                      | Adjusted mean difference     |
| Point estimate                          | -1.19                        |

Confidence interval

|                      |                            |
|----------------------|----------------------------|
| level                | 95 %                       |
| sides                | 2-sided                    |
| lower limit          | -2.13                      |
| upper limit          | -0.26                      |
| Variability estimate | Standard error of the mean |
| Dispersion value     | 0.465                      |

Notes:

[102] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                         |
|-----------------------------------|-------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 11 |
|-----------------------------------|-------------------------|

Statistical analysis description:

Japanese region: Analysis reported for change from baseline in DAS28 (CRP) at Day 85. Analysis Type used was dose escalation.

|   |                              |
|---|------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 140                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[103]</sup>       |
| P-value                                 | = 0.931                      |
| Method                                  | Repeated measures model      |
| Parameter estimate                      | Adjusted mean difference     |
| Point estimate                          | -0.04                        |

Confidence interval

|                      |                            |
|----------------------|----------------------------|
| level                | 95 %                       |
| sides                | 2-sided                    |
| lower limit          | -0.94                      |
| upper limit          | 0.86                       |
| Variability estimate | Standard error of the mean |
| Dispersion value     | 0.448                      |

Notes:

[103] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

| Statistical analysis title  | Statistical Analysis 12       |
|---|-------------------------------|
| Statistical analysis description:   |                               |
| Japanese region: Analysis reported for change from baseline in DAS28 (CRP) at Day 85. Analysis Type used was dose escalation. |                               |
| Comparison groups   | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis   | 139                           |
| Analysis specification  | Pre-specified                 |
| Analysis type   | other <sup>[104]</sup>        |
| P-value   | = 0.07                        |
| Method  | Repeated measures model       |
| Parameter estimate  | Adjusted mean difference      |
| Point estimate  | -0.86                         |
| Confidence interval   |                               |
| level   | 95 %                          |
| sides   | 2-sided                       |
| lower limit   | -1.8                          |
| upper limit   | 0.07                          |
| Variability estimate  | Standard error of the mean    |
| Dispersion value  | 0.465                         |

Notes:

[104] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

| Statistical analysis title  | Statistical Analysis 13                  |
|---|--|
| Statistical analysis description:   |  |
| Japanese region: Analysis reported for change from baseline in DAS28 (ESR) at Day 85. Analysis Type used was dose escalation. |  |
| Comparison groups   | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis   | 140                                      |
| Analysis specification  | Pre-specified                            |
| Analysis type   | other <sup>[105]</sup>                   |
| P-value   | = 0.854                                  |
| Method  | Repeated measures model                  |
| Parameter estimate  | Adjusted mean difference                 |
| Point estimate  | -0.08                                    |
| Confidence interval   |  |
| level   | 95 %                                     |
| sides   | 2-sided                                  |
| lower limit   | -0.99                                    |
| upper limit   | 0.82                                     |
| Variability estimate  | Standard error of the mean               |
| Dispersion value  | 0.449                                    |

Notes:

[105] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

| Statistical analysis title  | Statistical Analysis 14 |
|---|-------------------------|
| Statistical analysis description:   |                         |
| Japanese region: Analysis reported for change from baseline in DAS28 (ESR) at Day 85. Analysis Type used was dose escalation. |                         |

|   |                              |
|---|------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 141                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[106]</sup>       |
| P-value                                 | = 0.011                      |
| Method                                  | Repeated measures model      |
| Parameter estimate                      | Adjusted mean difference     |
| Point estimate                          | -1.25                        |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -2.19                        |
| upper limit                             | -0.31                        |
| Variability estimate                    | Standard error of the mean   |
| Dispersion value                        | 0.468                        |

Notes:

[106] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>   | Statistical Analysis 15      |
| Statistical analysis description:   |                              |
| Japanese region: Analysis reported for change from baseline in DAS28 (ESR) at Day 85. Analysis Type used was dose escalation. |                              |
| Comparison groups   | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis   | 140                          |
| Analysis specification  | Pre-specified                |
| Analysis type   | other <sup>[107]</sup>       |
| P-value   | = 0.271                      |
| Method  | Repeated measures model      |
| Parameter estimate  | Adjusted mean difference     |
| Point estimate  | -0.5                         |
| Confidence interval   |                              |
| level   | 95 %                         |
| sides   | 2-sided                      |
| lower limit   | -1.4                         |
| upper limit   | 0.4                          |
| Variability estimate  | Standard error of the mean   |
| Dispersion value  | 0.448                        |

Notes:

[107] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|   |                               |
|---|-------------------------------|
| <b>Statistical analysis title</b>   | Statistical Analysis 16       |
| Statistical analysis description:   |                               |
| Japanese region: Analysis reported for change from baseline in DAS28 (ESR) at Day 85. Analysis Type used was dose escalation. |                               |
| Comparison groups   | Placebo v Mavrilimumab 100 mg |

|   |                            |
|---|----------------------------|
| Number of subjects included in analysis | 139                        |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other <sup>[108]</sup>     |
| P-value                                 | = 0.031                    |
| Method                                  | Repeated measures model    |
| Parameter estimate                      | Adjusted mean difference   |
| Point estimate                          | -1.03                      |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | -1.97                      |
| upper limit                             | -0.1                       |
| Variability estimate                    | Standard error of the mean |
| Dispersion value                        | 0.465                      |

Notes:

[108] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

### Secondary: Percentage of Participants who Achieved DAS28 (CRP) and DAS28 (ESR) Remission at Day 85

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants who Achieved DAS28 (CRP) and DAS28 (ESR) Remission at Day 85 |
|-----------------|---|

End point description:

DAS28 calculated SJC and TJC using the 28 joints, GH using participant assessment of disease activity (participant rated arthritis activity using the numerical rating scale with 0 = best, 10 = worst) and CRP (mg/L) for DAS28 (CRP) or ESR (mm/hour) for DAS28 (ESR). Total score range: 0-9.4, higher score = more disease activity. DAS28 <3.2 = low disease activity, >=3.2 to 5.1 = moderate to high disease activity and <2.6= remission. Remission was defined as less than 2.6 DAS28 (ESR) or DAS28 (CRP) score. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues.

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

End point timeframe:

Day 85

| End point values   | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|--|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type   | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed                                  | 48                                   | 49                    | 48                    | 47                     |
| Units: percentage of participants<br>number (not applicable) |                                      |                       |                       |                        |
| DAS28(CRP)   | 14.6                                 | 22.4                  | 18.8                  | 23.4                   |
| DAS28(ESR)   | 6.3                                  | 8.2                   | 8.3                   | 6.4                    |

| End point values                  | Placebo         |  |  |  |
|-----------------------------------|-----------------|--|--|--|
| Subject group type                | Reporting group |  |  |  |
| Number of subjects analysed       | 92              |  |  |  |
| Units: percentage of participants |                 |  |  |  |

|                         |     |  |  |  |
|-------------------------|-----|--|--|--|
| number (not applicable) |     |  |  |  |
| DAS28(CRP)              | 7.6 |  |  |  |
| DAS28(ESR)              | 3.3 |  |  |  |

## Statistical analyses

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 1 |
|-----------------------------------|------------------------|

Statistical analysis description:

DAS28 (CRP): p-value was calculated using a two-tailed Fisher's exact test. Analysis Type used was dose escalation.

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 140                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[109]</sup>                   |
| P-value                                 | = 0.238                                  |
| Method                                  | Fisher exact                             |
| Parameter estimate                      | Percent difference                       |
| Point estimate                          | 7  |
| Confidence interval                     |  |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | -3.3                                     |
| upper limit                             | 20.5                                     |

Notes:

[109] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 2 |
|-----------------------------------|------------------------|

Statistical analysis description:

DAS28 (CRP): p-value was calculated using a two-tailed Fisher's exact test. Analysis Type used was dose escalation.

|   |                              |
|---|------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 141                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[110]</sup>       |
| P-value                                 | = 0.017                      |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 14.8                         |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | 2.8                          |
| upper limit                             | 29.7                         |

Notes:

[110] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

DAS28 (CRP): p-value was calculated using a two-tailed Fisher's exact test. Analysis Type used was



dose escalation.

|   |                              |
|---|------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 140                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[111]</sup>       |
| P-value                                 | = 0.09                       |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 11.1                         |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | 0                            |
| upper limit                             | 25.4                         |

Notes:

[111] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

DAS28 (CRP): p-value was calculated using a two-tailed Fisher's exact test. Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 139                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[112]</sup>        |
| P-value                                 | = 0.015                       |
| Method                                  | Fisher exact                  |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | 15.8                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 2.9                           |
| upper limit                             | 31                            |

Notes:

[112] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 5 |
|-----------------------------------|------------------------|

Statistical analysis description:

DAS28 (ESR): p-value was calculated using a two-tailed Fisher's exact test. Analysis Type used was dose escalation.

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 140                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[113]</sup>                   |
| P-value                                 | = 0.412                                  |
| Method                                  | Fisher exact                             |
| Parameter estimate                      | Percent difference                       |
| Point estimate                          | 3  |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -4.2    |
| upper limit         | 14      |

Notes:

[113] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 6 |
|-----------------------------------|------------------------|

Statistical analysis description:

DAS28 (ESR): p-value was calculated using a two-tailed Fisher's exact test. Analysis Type used was dose escalation.

|   |                              |
|---|------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 141                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[114]</sup>       |
| P-value                                 | = 0.237                      |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 4.9                          |

Confidence interval

|             |         |
|-------------|---------|
| level       | 95 %    |
| sides       | 2-sided |
| lower limit | -2.9    |
| upper limit | 16.4    |

Notes:

[114] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 7 |
|-----------------------------------|------------------------|

Statistical analysis description:

DAS28 (ESR): p-value was calculated using a two-tailed Fisher's exact test. Analysis Type used was dose escalation.

|   |                              |
|---|------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 140                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[115]</sup>       |
| P-value                                 | = 0.231                      |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 5.1                          |

Confidence interval

|             |         |
|-------------|---------|
| level       | 95 %    |
| sides       | 2-sided |
| lower limit | -2.8    |
| upper limit | 16.8    |

Notes:

[115] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 8 |
|-----------------------------------|------------------------|

Statistical analysis description:

DAS28 (ESR): p-value was calculated using a two-tailed Fisher's exact test. Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 139                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[116]</sup>        |
| P-value                                 | = 0.406                       |
| Method                                  | Fisher exact                  |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | 3.1                           |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -4.1                          |
| upper limit                             | 14.4                          |

Notes:

[116] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

**Secondary: Percentage of Participants who Achieved DAS28 (CRP) and DAS28 (ESR) Remission at Day 85 by Region**

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants who Achieved DAS28 (CRP) and DAS28 (ESR) Remission at Day 85 by Region |
|-----------------|---|

End point description:

DAS28 calculated SJC and TJC using the 28 joints, GH using participant assessment of disease activity (participant rated arthritis activity using the numerical rating scale with 0 = best, 10 = worst) and CRP (mg/L) for DAS28 (CRP) or ESR (mm/hour) for DAS28 (ESR). Total score range: 0-9.4, higher score = more disease activity. DAS28 <3.2 = low disease activity, >=3.2 to 5.1 = moderate to high disease activity and <2.6= remission. Remission was defined as less than 2.6 DAS28 (ESR) or DAS28 (CRP) score. DAS28 (CRP) and DAS28 (ESR) for the European and Japanese regions were reported. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues. Here "n" signifies participants who were evaluable for this measure for the specified region for each arm, respectively.

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

End point timeframe:

Day 85

| End point values                           | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|--|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                         | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed                | 48                                   | 49                    | 48                    | 47                     |
| Units: percentage of participants          |                                      |                       |                       |                        |
| number (not applicable)                    |                                      |                       |                       |                        |
| European:<br>DAS28(CRP):(n=75,39,41,39,39) | 15.4                                 | 17.1                  | 17.9                  | 23.1                   |
| European:<br>DAS28(ESR):(n=75,39,41,39,39) | 7.7                                  | 9.8                   | 7.7                   | 7.7                    |
| Japanese: DAS28(CRP) (n=17,9,8,9,8)        | 11.1                                 | 50                    | 22.2                  | 25                     |
| Japanese: DAS28(ESR) (n=17,9,8,9,8)        | 0                                    | 0                     | 11.1                  | 0                      |

| <b>End point values</b>                     | Placebo         |  |  |  |
|---|-----------------|--|--|--|
| Subject group type                          | Reporting group |  |  |  |
| Number of subjects analysed                 | 92              |  |  |  |
| Units: percentage of participants           |                 |  |  |  |
| number (not applicable)                     |                 |  |  |  |
| European:<br>DAS28(CRP): (n=75,39,41,39,39) | 6.7             |  |  |  |
| European:<br>DAS28(ESR): (n=75,39,41,39,39) | 1.3             |  |  |  |
| Japanese: DAS28(CRP) (n=17,9,8,9,8)         | 11.8            |  |  |  |
| Japanese: DAS28(ESR) (n=17,9,8,9,8)         | 11.8            |  |  |  |

## Statistical analyses

| <b>Statistical analysis title</b>  | Statistical Analysis 1                   |
|--|--|
| Statistical analysis description:<br>Analysis Type used was dose escalation. |  |
| Comparison groups  | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis                                      | 140                                      |
| Analysis specification   | Pre-specified                            |
| Analysis type  | other <sup>[117]</sup>                   |
| P-value  | = 0.182 <sup>[118]</sup>                 |
| Method   | Fisher exact                             |
| Parameter estimate   | Percent difference                       |
| Point estimate   | 8.7                                      |
| Confidence interval  |  |
| level  | 95 %                                     |
| sides  | 2-sided                                  |
| lower limit  | -2.7                                     |
| upper limit  | 24.4                                     |

Notes:

[117] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[118] - European region (DAS28 [CRP]): p-value was calculated using a two-tailed Fisher's exact test.

| <b>Statistical analysis title</b>  | Statistical Analysis 2       |
|--|------------------------------|
| Statistical analysis description:<br>Analysis Type used was dose escalation. |                              |
| Comparison groups  | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis                                      | 141                          |
| Analysis specification   | Pre-specified                |
| Analysis type  | other <sup>[119]</sup>       |
| P-value  | = 0.11 <sup>[120]</sup>      |
| Method   | Fisher exact                 |
| Parameter estimate   | Percent difference           |
| Point estimate   | 10.4                         |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -1.2    |
| upper limit         | 25.5    |

Notes:

[119] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[120] - European region (DAS28 [CRP]): p-value was calculated using a two-tailed Fisher's exact test.

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 3       |
| Statistical analysis description:       |                              |
| Analysis Type used was dose escalation. |                              |
| Comparison groups                       | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 140                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[121]</sup>       |
| P-value                                 | = 0.104 <sup>[122]</sup>     |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 11.3                         |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -0.6                         |
| upper limit                             | 26.9                         |

Notes:

[121] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[122] - European region (DAS28 [CRP]): p-value was calculated using a two-tailed Fisher's exact test.

|   |                               |
|---|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 4        |
| Statistical analysis description:       |                               |
| Analysis Type used was dose escalation. |                               |
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 139                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[123]</sup>        |
| P-value                                 | = 0.016 <sup>[124]</sup>      |
| Method                                  | Fisher exact                  |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | 16.4                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 3.5                           |
| upper limit                             | 32.7                          |

Notes:

[123] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[124] - European region (DAS28 [CRP]): p-value was calculated using a two-tailed Fisher's exact test.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 5 |
|-----------------------------------|------------------------|

|   |   |
|---|---|
| Statistical analysis description:       |   |
| Analysis Type used was dose escalation. |   |
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) v Mavrilimumab 50 mg v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 235   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other <sup>[125]</sup>  |
| P-value                                 | = 0.115 <sup>[126]</sup>  |
| Method                                  | Fisher exact  |
| Parameter estimate                      | Percent difference  |
| Point estimate                          | 6.4   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -1  |
| upper limit                             | 19.3  |

Notes:

[125] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[126] - European region (DAS28 [ESR]): p-value was calculated using a two-tailed Fisher's exact test.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 6 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis Type used was dose escalation.

|   |                              |
|---|------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 141                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[127]</sup>       |
| P-value                                 | = 0.052 <sup>[128]</sup>     |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 8.4                          |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | 0.6                          |
| upper limit                             | 21.6                         |

Notes:

[127] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[128] - European region (DAS28 [ESR]): p-value was calculated using a two-tailed Fisher's exact test.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 7 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis Type used was dose escalation.

|                   |   |
|-------------------|---|
| Comparison groups | Placebo v Mavrilimumab 10 milligram (mg) v Mavrilimumab 50 mg v Mavrilimumab 100 mg |
|-------------------|---|

|   |                          |
|---|--------------------------|
| Number of subjects included in analysis | 235                      |
| Analysis specification                  | Pre-specified            |
| Analysis type                           | other <sup>[129]</sup>   |
| P-value                                 | = 0.115 <sup>[130]</sup> |
| Method                                  | Fisher exact             |
| Parameter estimate                      | Percent difference       |
| Point estimate                          | 6.4                      |
| Confidence interval                     |                          |
| level                                   | 95 %                     |
| sides                                   | 2-sided                  |
| lower limit                             | -1                       |
| upper limit                             | 19.3                     |

Notes:

[129] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[130] - European region (DAS28 [ESR]): p-value was calculated using a two-tailed Fisher's exact test.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 8 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis Type used was dose escalation.

|   |   |
|---|---|
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) v Mavrilimumab 50 mg v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 235   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other <sup>[131]</sup>  |
| P-value                                 | = 0.115 <sup>[132]</sup>  |
| Method                                  | Fisher exact  |
| Parameter estimate                      | Percent difference  |
| Point estimate                          | 6.4   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -1  |
| upper limit                             | 19.3  |

Notes:

[131] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[132] - European region (DAS28 [ESR]): p-value was calculated using a two-tailed Fisher's exact test.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 9 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis Type used was dose escalation.

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 140                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[133]</sup>                   |
| P-value                                 | = 1 <sup>[134]</sup>                     |
| Method                                  | Fisher exact                             |
| Parameter estimate                      | Percent difference                       |
| Point estimate                          | -0.7                                     |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -27     |
| upper limit         | 34.8    |

Notes:

[133] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[134] - Japanese region (DAS28 [CRP]): p-value was calculated using a two-tailed Fisher's exact test.

|                                   |                         |
|-----------------------------------|-------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 10 |
|-----------------------------------|-------------------------|

Statistical analysis description:

Analysis Type used was dose escalation.

|   |                              |
|---|------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 141                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[135]</sup>       |
| P-value                                 | = 0.059 <sup>[136]</sup>     |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 38.2                         |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | 1.6                          |
| upper limit                             | 71.2                         |

Notes:

[135] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[136] - Japanese region (DAS28 [CRP]): p-value was calculated using a two-tailed Fisher's exact test.

|                                   |                         |
|-----------------------------------|-------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 11 |
|-----------------------------------|-------------------------|

Statistical analysis description:

Analysis Type used was dose escalation.

|   |                              |
|---|------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 140                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[137]</sup>       |
| P-value                                 | = 0.591 <sup>[138]</sup>     |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 10.5                         |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -18.2                        |
| upper limit                             | 46.2                         |

Notes:

[137] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[138] - Japanese region (DAS28 [CRP]): p-value was calculated using a two-tailed Fisher's exact test.

|                                   |                         |
|-----------------------------------|-------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 12 |
|-----------------------------------|-------------------------|



|   |                               |
|---|-------------------------------|
| Statistical analysis description:       |                               |
| Analysis Type used was dose escalation. |                               |
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 139                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[139]</sup>        |
| P-value                                 | = 0.57 <sup>[140]</sup>       |
| Method                                  | Fisher exact                  |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | 13.2                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -16.6                         |
| upper limit                             | 51.4                          |

Notes:

[139] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[140] - Japanese region (DAS28 [CRP]): p-value was calculated using a two-tailed Fisher's exact test.

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Statistical Analysis 13                  |
| Statistical analysis description:       |  |
| Analysis Type used was dose escalation. |  |
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 140                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[141]</sup>                   |
| P-value                                 | = 0.529 <sup>[142]</sup>                 |
| Method                                  | Fisher exact                             |
| Parameter estimate                      | Percent difference                       |
| Point estimate                          | -11.8                                    |
| Confidence interval                     |  |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | -35                                      |
| upper limit                             | 22.7                                     |

Notes:

[141] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[142] - Japanese region (DAS28 [ESR]): p-value was calculated using a two-tailed Fisher's exact test.

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Statistical Analysis 14                            |
| Statistical analysis description:       |  |
| Analysis Type used was dose escalation. |  |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 188  |
| Analysis specification                  | Pre-specified                                      |
| Analysis type                           | other <sup>[143]</sup>                             |
| P-value                                 | = 1 <sup>[144]</sup>                               |
| Method                                  | Fisher exact                                       |
| Parameter estimate                      | Percent difference                                 |
| Point estimate                          | -11.8  |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -37.5   |
| upper limit         | 22.6    |

Notes:

[143] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[144] - Japanese region (DAS28 [ESR]): p-value was calculated using a two-tailed Fisher's exact test.

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 15      |
| Statistical analysis description:       |                              |
| Analysis Type used was dose escalation. |                              |
| Comparison groups                       | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 140                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[145]</sup>       |
| P-value                                 | = 1 <sup>[146]</sup>         |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | -0.7                         |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -27                          |
| upper limit                             | 34.8                         |

Notes:

[145] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[146] - Japanese region (DAS28 [ESR]): p-value was calculated using a two-tailed Fisher's exact test.

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Statistical Analysis 16                            |
| Statistical analysis description:       |  |
| Analysis Type used was dose escalation. |  |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 188  |
| Analysis specification                  | Pre-specified                                      |
| Analysis type                           | other <sup>[147]</sup>                             |
| P-value                                 | = 1 <sup>[148]</sup>                               |
| Method                                  | Fisher exact                                       |
| Parameter estimate                      | Percent difference                                 |
| Point estimate                          | -11.8  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -37.5  |
| upper limit                             | 22.6   |

Notes:

[147] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

[148] - Japanese region (DAS28 [ESR]): p-value was calculated using a two-tailed Fisher's exact test.

## Secondary: Time to Onset for DAS28 (CRP) and DAS (ESR) Response and Remission

|  |  |
|--|--|
| End point title  | Time to Onset for DAS28 (CRP) and DAS (ESR) Response and Remission |
| End point description:<br>DAS28 calculated SJC and TJC using the 28 joints, GH using participant assessment of disease activity (participant rated arthritis activity using the numerical rating scale with 0 = best, 10 = worst) and CRP (mg/L) for DAS28 (CRP) or ESR (mm/hour) for DAS28 (ESR). Total score range: 0-9.4, higher score = more disease activity. DAS28 <3.2 = low disease activity, >=3.2 to 5.1 = moderate to high disease activity and <2.6= remission. Response was defined as 1.2 decrease from baseline in DAS28 (CRP) or DAS28 (ESR) score. Remission was defined as less than 2.6 DAS28 (CRP) or DAS28 (ESR) score. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues. |  |
| End point type   | Secondary  |
| End point timeframe:<br>Baseline up to Day 169 (follow-up)   |  |

| End point values                 | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg   | Mavrilimumab<br>50 mg   | Mavrilimumab<br>100 mg  |
|----------------------------------|--------------------------------------|-------------------------|-------------------------|-------------------------|
| Subject group type               | Reporting group                      | Reporting group         | Reporting group         | Reporting group         |
| Number of subjects analysed      | 48                                   | 49                      | 48                      | 47                      |
| Units: days                      |                                      |                         |                         |                         |
| median (confidence interval 95%) |                                      |                         |                         |                         |
| DAS28 (CRP) Response             | 84 (43 to 99999)                     | 43 (29 to 58)           | 71 (42 to 89)           | 42 (29 to 45)           |
| DAS28 (CRP) Remission            | 99999 (-99999 to 99999)              | 99999 (99999 to 99999)  | 99999 (-99999 to 99999) | 99999 (-99999 to 99999) |
| DAS28 (ESR) Response             | 58 (43 to 86)                        | 30 (29 to 43)           | 57 (29 to 71)           | 29 (28 to 42)           |
| DAS28 (ESR) Remission            | 99999 (-99999 to 99999)              | 99999 (-99999 to 99999) | 99999 (-99999 to 99999) | 99999 (-99999 to 99999) |

| End point values                 | Placebo                 |  |  |  |
|----------------------------------|-------------------------|--|--|--|
| Subject group type               | Reporting group         |  |  |  |
| Number of subjects analysed      | 92                      |  |  |  |
| Units: days                      |                         |  |  |  |
| median (confidence interval 95%) |                         |  |  |  |
| DAS28 (CRP) Response             | 88 (57 to 88)           |  |  |  |
| DAS28 (CRP) Remission            | 99999 (-99999 to 99999) |  |  |  |
| DAS28 (ESR) Response             | 85 (57 to 88)           |  |  |  |
| DAS28 (ESR) Remission            | 99999 (-99999 to 99999) |  |  |  |

## Statistical analyses

|  |                        |
|--|------------------------|
| Statistical analysis title   | Statistical Analysis 1 |
| Statistical analysis description:<br>Analysis reported for DAS28 (CRP) response. Analysis Type used was dose escalation. |                        |

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 140                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other                                    |
| P-value                                 | = 0.604                                  |
| Method                                  | Logrank                                  |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 2 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis reported for DAS28 (CRP) response. Analysis Type used was dose escalation.

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 188  |
| Analysis specification                  | Pre-specified                                      |
| Analysis type                           | other  |
| P-value                                 | < 0.001  |
| Method                                  | Logrank  |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis reported for DAS28 (CRP) response. Analysis Type used was dose escalation.

|   |                              |
|---|------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 140                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other                        |
| P-value                                 | = 0.145                      |
| Method                                  | Logrank                      |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis reported for DAS28 (CRP) response. Analysis Type used was dose escalation.

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 188  |
| Analysis specification                  | Pre-specified                                      |
| Analysis type                           | other  |
| P-value                                 | < 0.001  |
| Method                                  | Logrank  |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 5 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis reported for DAS28 (ESR) response. Analysis Type used was dose escalation.

|                   |  |
|-------------------|--|
| Comparison groups | Placebo v Mavrilimumab 10 milligram (mg) |
|-------------------|--|

|   |               |
|---|---------------|
| Number of subjects included in analysis | 140           |
| Analysis specification                  | Pre-specified |
| Analysis type                           | other         |
| P-value                                 | = 0.282       |
| Method                                  | Logrank       |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 6 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis reported for DAS28 (ESR) response. Analysis Type used was dose escalation.

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 188  |
| Analysis specification                  | Pre-specified                                      |
| Analysis type                           | other  |
| P-value                                 | < 0.001  |
| Method                                  | Logrank  |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 7 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis reported for DAS28 (ESR) response. Analysis Type used was dose escalation.

|   |                              |
|---|------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 140                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other                        |
| P-value                                 | = 0.047                      |
| Method                                  | Logrank                      |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 8 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis reported for DAS28 (ESR) response. Analysis Type used was dose escalation.

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 188  |
| Analysis specification                  | Pre-specified                                      |
| Analysis type                           | other  |
| P-value                                 | < 0.001  |
| Method                                  | Logrank  |

## **Secondary: Time to Onset for DAS28 (CRP) and DAS (ESR) Response and Remission by Region**

|                 |  |
|-----------------|--|
| End point title | Time to Onset for DAS28 (CRP) and DAS (ESR) Response and Remission by Region |
|-----------------|--|

**End point description:**

DAS28 calculated SJC and TJC using the 28 joints,GH using participant assessment of disease activity (participant rated arthritis activity using the numerical rating scale with 0=best,10=worst) and CRP(mg/L) for DAS28(CRP)orESR(mm/hour) for DAS28(ESR). Total score range:0-9.4, higher score=more disease activity.DAS28<3.2=low disease activity,>=3.2 to 5.1=moderate to high disease activity and<2.6=remission.Response was defined as 1.2 decrease from baseline in DAS28(CRP)orDAS28(ESR) score. Remission was defined as <2.6 DAS28(CRP)orDAS28(ESR) score. Time to response for DAS28(CRP) and DAS28(ESR) by region were reported. Time to remission for DAS28(CRP) and DAS28(ESR) by region were not analyzed because time to remission for the overall study population could not be achieved. The ITT population was analysed and six participants were excluded for data integrity issues. Here "n" signifies participants who were evaluable for this measure for the specified region for each arm, respectively.

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

End point timeframe:

Baseline up to Day 169 (follow-up)

| End point values                                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|--|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                                   | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed                          | 48                                   | 49                    | 48                    | 47                     |
| Units: days  |                                      |                       |                       |                        |
| median (confidence interval 95%)                     |                                      |                       |                       |                        |
| European: DAS28 (CRP) Response<br>(n=75,39,41,39,39) | 43 (43 to 99999)                     | 43 (42 to 71)         | 50 (29 to 89)         | 42 (29 to 57)          |
| Japanese: DAS28 (CRP) Response<br>(n=17,9,8,9,8)     | 99999 (-99999 to 99999)              | 22.5 (15 to 57)       | 87 (30 to 87)         | 37 (15 to 57)          |
| European: DAS28 (ESR) Response<br>(n=75,39,41,39,39) | 57 (30 to 85)                        | 42 (29 to 43)         | 52.5 (29 to 84)       | 29 (28 to 42)          |
| Japanese: DAS28 (ESR) Response<br>(n=17,9,8,9,8)     | 86 (57 to 86)                        | 29 (15 to 44)         | 44.5 (29 to 99999)    | 30 (15 to 44)          |

| End point values                                     | Placebo                 |  |  |  |
|--|-------------------------|--|--|--|
| Subject group type                                   | Reporting group         |  |  |  |
| Number of subjects analysed                          | 92                      |  |  |  |
| Units: days  |                         |  |  |  |
| median (confidence interval 95%)                     |                         |  |  |  |
| European: DAS28 (CRP) Response<br>(n=75,39,41,39,39) | 85 (57 to 88)           |  |  |  |
| Japanese: DAS28 (CRP) Response<br>(n=17,9,8,9,8)     | 99999 (-99999 to 99999) |  |  |  |
| European: DAS28 (ESR) Response<br>(n=75,39,41,39,39) | 71 (57 to 88)           |  |  |  |
| Japanese: DAS28 (ESR) Response<br>(n=17,9,8,9,8)     | 99999 (-99999 to 99999) |  |  |  |

**Statistical analyses**

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Statistical Analysis 1                   |
| Statistical analysis description:  |  |
| European region: Analysis reported for DAS28 (CRP) response. Analysis Type used was dose escalation. |  |
| Comparison groups  | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis  | 140                                      |
| Analysis specification   | Pre-specified                            |
| Analysis type  | other                                    |
| P-value  | = 0.237                                  |
| Method   | Logrank                                  |

|  |                              |
|--|------------------------------|
| <b>Statistical analysis title</b>  | Statistical Analysis 2       |
| Statistical analysis description:  |                              |
| European region: Analysis reported for DAS28 (CRP) response. Analysis Type used was dose escalation. |                              |
| Comparison groups  | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis  | 141                          |
| Analysis specification   | Pre-specified                |
| Analysis type  | other                        |
| P-value  | = 0.005                      |
| Method   | Logrank                      |

|  |                              |
|--|------------------------------|
| <b>Statistical analysis title</b>  | Statistical Analysis 3       |
| Statistical analysis description:  |                              |
| European region: Analysis reported for DAS28 (CRP) response. Analysis Type used was dose escalation. |                              |
| Comparison groups  | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis  | 140                          |
| Analysis specification   | Pre-specified                |
| Analysis type  | other                        |
| P-value  | = 0.134                      |
| Method   | Logrank                      |

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Statistical Analysis 5                   |
| Statistical analysis description:  |  |
| Japanese region: Analysis reported for DAS28 (CRP) response. Analysis Type used was dose escalation. |  |
| Comparison groups  | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis  | 140                                      |
| Analysis specification   | Pre-specified                            |
| Analysis type  | other                                    |
| P-value  | = 0.265                                  |
| Method   | Logrank                                  |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

European region: Analysis reported for DAS28 (CRP) response. Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 139                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 0.001                       |
| Method                                  | Logrank                       |

---

**Statistical analysis title**

Statistical Analysis 6

Statistical analysis description:

Japanese region: Analysis reported for DAS28 (CRP) response. Analysis Type used was dose escalation.

|   |                              |
|---|------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 141                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other                        |
| P-value                                 | = 0.013                      |
| Method                                  | Logrank                      |

---

**Statistical analysis title**

Statistical Analysis 7

Statistical analysis description:

Japanese region: Analysis reported for DAS28 (CRP) response. Analysis Type used was dose escalation.

|   |                              |
|---|------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 140                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other                        |
| P-value                                 | = 0.952                      |
| Method                                  | Logrank                      |

---

**Statistical analysis title**

Statistical Analysis 9

Statistical analysis description:

European region: Analysis reported for DAS28 (ESR) response. Analysis Type used was dose escalation.

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 140                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other                                    |
| P-value                                 | = 0.246                                  |
| Method                                  | Logrank                                  |

---

**Statistical analysis title**

Statistical Analysis 10



Statistical analysis description:

European region: Analysis reported for DAS28 (ESR) response. Analysis Type used was dose escalation.

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 188  |
| Analysis specification                  | Pre-specified                                      |
| Analysis type                           | other  |
| P-value                                 | < 0.001  |
| Method                                  | Logrank  |

---

**Statistical analysis title**

Statistical Analysis 8

Statistical analysis description:

Japanese region: Analysis reported for DAS28 (CRP) response. Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 139                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | = 0.004                       |
| Method                                  | Logrank                       |

---

**Statistical analysis title**

Statistical Analysis 11

Statistical analysis description:

European region: Analysis reported for DAS28 (ESR) response. Analysis Type used was dose escalation.

|   |                              |
|---|------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 140                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other                        |
| P-value                                 | = 0.126                      |
| Method                                  | Logrank                      |

---

**Statistical analysis title**

Statistical Analysis 12

Statistical analysis description:

European region: Analysis reported for DAS28 (ESR) response. Analysis Type used was dose escalation.

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 188  |
| Analysis specification                  | Pre-specified                                      |
| Analysis type                           | other  |
| P-value                                 | < 0.001  |
| Method                                  | Logrank  |

---

**Statistical analysis title**

Statistical Analysis 15

Statistical analysis description:

Japanese region: Analysis reported for DAS28 (ESR) response. Analysis Type used was dose escalation.

|   |                              |
|---|------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 140                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other                        |
| P-value                                 | = 0.125                      |
| Method                                  | Logrank                      |

---

**Statistical analysis title**

Statistical Analysis 14

Statistical analysis description:

Japanese region: Analysis reported for DAS28 (ESR) response. Analysis Type used was dose escalation.

|   |                              |
|---|------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 141                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other                        |
| P-value                                 | = 0.005                      |
| Method                                  | Logrank                      |

---

**Statistical analysis title**

Statistical Analysis 13

Statistical analysis description:

Japanese region: Analysis reported for DAS28 (ESR) response. Analysis Type used was dose escalation.

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 140                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other                                    |
| P-value                                 | = 0.831                                  |
| Method                                  | Logrank                                  |

---

**Statistical analysis title**

Statistical Analysis 16

Statistical analysis description:

Japanese region: Analysis reported for DAS28 (ESR) response. Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 139                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 0.001                       |
| Method                                  | Logrank                       |

---

**Secondary: Duration of DAS28 (CRP) and DAS28 (ESR) Response and Remission**

|                 |  |
|-----------------|--|
| End point title | Duration of DAS28 (CRP) and DAS28 (ESR) Response and |
|-----------------|--|

## End point description:

DAS28 calculated SJC and TJC using 28 joints, GH using participant assessment of disease activity (participant rated arthritis activity using numerical rating scale with 0=best, 10=worst) and CRP (mg/L) for DAS28 (CRP) or ESR (mm/hour) for DAS28 (ESR). Total score range: 0-9.4, higher score = more disease activity. DAS28 < 3.2 = low disease activity, >= 3.2 to 5.1 = moderate to high disease activity and < 2.6 = remission. Response defined as 1.2 decrease from baseline in DAS28 (CRP) or DAS28 (ESR) score. Remission defined as < 2.6 DAS28 (CRP) or DAS28 (ESR) score. Expected duration of response (DOR) calculated as response rate (in percentage) multiplied by mean DOR (in days) by using Weibull Model. Duration of DAS28 (CRP) and DAS28 (ESR) remission were not analyzed because very few participants achieved remission in the overall study population. ITT population (6 participants were excluded for data integrity issues). Here "n" signifies participants who were evaluable for this measure for specified parameter for each arm, respectively.

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

End point timeframe:

Baseline up to Day 169

| End point values            | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|-----------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type          | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed | 48                                   | 49                    | 48                    | 47                     |
| Units: Percentage of days   |                                      |                       |                       |                        |
| number (not applicable)     |                                      |                       |                       |                        |
| DAS28 (CRP) Response        | 42.19                                | 81.89                 | 54.8                  | 83.07                  |
| DAS28 (ESR) Response        | 52.96                                | 71.14                 | 75.97                 | 96.52                  |

| End point values            | Placebo         |  |  |  |
|-----------------------------|-----------------|--|--|--|
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 92              |  |  |  |
| Units: Percentage of days   |                 |  |  |  |
| number (not applicable)     |                 |  |  |  |
| DAS28 (CRP) Response        | 43.4            |  |  |  |
| DAS28 (ESR) Response        | 46.11           |  |  |  |

## Statistical analyses

|                            |                        |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

Analysis reported for DAS28 (ESR) response. Analysis Type used was dose escalation.

|                   |  |
|-------------------|--|
| Comparison groups | Placebo v Mavrilimumab 10 milligram (mg) |
|-------------------|--|

|   |  |
|---|--|
| Number of subjects included in analysis | 140                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[149]</sup>                   |
| P-value                                 | = 0.486                                  |
| Method                                  | Exponential,Weibull and Log normal model |
| Parameter estimate                      | Ratio of expected duration of response   |
| Point estimate                          | 1.15                                     |
| Confidence interval                     |  |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | 0.78                                     |
| upper limit                             | 1.69                                     |

Notes:

[149] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 2 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis reported for DAS28 (ESR) response. Analysis Type used was dose escalation.

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg             |
| Number of subjects included in analysis | 141                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[150]</sup>                   |
| P-value                                 | = 0.015                                  |
| Method                                  | Exponential,Weibull and Log normal model |
| Parameter estimate                      | Ratio of expected duration of response   |
| Point estimate                          | 1.54                                     |
| Confidence interval                     |  |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | 1.09                                     |
| upper limit                             | 2.18                                     |

Notes:

[150] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis reported for DAS28 (ESR) response. Analysis Type used was dose escalation.

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 50 mg             |
| Number of subjects included in analysis | 140                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[151]</sup>                   |
| P-value                                 | = 0.006                                  |
| Method                                  | Exponential,Weibull and Log normal model |
| Parameter estimate                      | Ratio of expected duration of response   |
| Point estimate                          | 1.65                                     |
| Confidence interval                     |  |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | 1.15                                     |
| upper limit                             | 2.36                                     |

Notes:

[151] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | Statistical Analysis 4                   |
| Statistical analysis description:   |  |
| Analysis reported for DAS28 (ESR) response. Analysis Type used was dose escalation. |  |
| Comparison groups   | Placebo v Mavrilimumab 100 mg            |
| Number of subjects included in analysis   | 139                                      |
| Analysis specification  | Pre-specified                            |
| Analysis type   | other <sup>[152]</sup>                   |
| P-value   | < 0.001                                  |
| Method  | Exponential,Weibull and Log normal model |
| Parameter estimate  | Ratio of expected duration of response   |
| Point estimate  | 2.09                                     |
| Confidence interval   |  |
| level   | 95 %                                     |
| sides   | 2-sided                                  |
| lower limit   | 1.49                                     |
| upper limit   | 2.93                                     |

Notes:

[152] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | Statistical Analysis 5                   |
| Statistical analysis description:   |  |
| Analysis reported for DAS28 (CRP) response. Analysis Type used was dose escalation. |  |
| Comparison groups   | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis   | 140                                      |
| Analysis specification  | Pre-specified                            |
| Analysis type   | other <sup>[153]</sup>                   |
| P-value   | = 0.906                                  |
| Method  | Exponential,Weibull and Log normal model |
| Parameter estimate  | Ratio of expected duration of response   |
| Point estimate  | 0.97                                     |
| Confidence interval   |  |
| level   | 95 %                                     |
| sides   | 2-sided                                  |
| lower limit   | 0.61                                     |
| upper limit   | 1.55                                     |

Notes:

[153] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>   | Statistical Analysis 6       |
| Statistical analysis description:   |                              |
| Analysis reported for DAS28 (CRP) response. Analysis Type used was dose escalation. |                              |
| Comparison groups   | Placebo v Mavrilimumab 30 mg |

|   |  |
|---|--|
| Number of subjects included in analysis | 141                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[154]</sup>                   |
| P-value                                 | < 0.001                                  |
| Method                                  | Exponential,Weibull and Log normal model |
| Parameter estimate                      | Ratio of expected duration of response   |
| Point estimate                          | 1.89                                     |
| Confidence interval                     |  |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | 1.31                                     |
| upper limit                             | 2.71                                     |

Notes:

[154] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 7 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis reported for DAS28 (CRP) response. Analysis Type used was dose escalation.

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 50 mg             |
| Number of subjects included in analysis | 140                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[155]</sup>                   |
| P-value                                 | = 0.272                                  |
| Method                                  | Exponential,Weibull and Log normal model |
| Parameter estimate                      | Ratio of expected duration of response   |
| Point estimate                          | 1.26                                     |
| Confidence interval                     |  |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | 0.83                                     |
| upper limit                             | 1.91                                     |

Notes:

[155] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 8 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis reported for DAS28 (CRP) response. Analysis Type used was dose escalation.

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 100 mg            |
| Number of subjects included in analysis | 139                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[156]</sup>                   |
| P-value                                 | < 0.001                                  |
| Method                                  | Exponential,Weibull and Log normal model |
| Parameter estimate                      | Ratio of expected duration of response   |
| Point estimate                          | 1.91                                     |
| Confidence interval                     |  |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | 1.34                                     |
| upper limit                             | 2.72                                     |

Notes:

[156] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

## Secondary: Percentage of Participants who Achieved American College of Rheumatology 20 (ACR20), ACR50 and ACR70 Responses at Day 85

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants who Achieved American College of Rheumatology 20 (ACR20), ACR50 and ACR70 Responses at Day 85 |
|-----------------|--|

End point description:

ACR20, ACR50, and ACR70, were defined as greater than or equal to ( $\geq$ ) 20 percent (%),  $\geq$ 50%, or  $\geq$ 70% improvement, respectively, in: swollen joint count and tender joint count and  $\geq$ 20%,  $\geq$ 50%, or  $\geq$ 70% improvement, respectively, in at least 3 of 5 remaining ACR core measures: participant assessment of pain; participant global assessment of disease activity; physician global assessment of disease activity; self-assessed disability (disability index of the Health Assessment Questionnaire [HAQ]); and C-Reactive Protein (CRP). The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Day 85               |           |

| End point values                  | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|-----------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed       | 48                                   | 49                    | 48                    | 47                     |
| Units: percentage of participants |                                      |                       |                       |                        |
| number (not applicable)           |                                      |                       |                       |                        |
| ACR20                             | 41.7                                 | 57.1                  | 37.5                  | 70.2                   |
| ACR50                             | 20.8                                 | 30.6                  | 16.7                  | 34                     |
| ACR70                             | 4.2                                  | 10.2                  | 6.3                   | 14.9                   |

| End point values                  | Placebo         |  |  |  |
|-----------------------------------|-----------------|--|--|--|
| Subject group type                | Reporting group |  |  |  |
| Number of subjects analysed       | 92              |  |  |  |
| Units: percentage of participants |                 |  |  |  |
| number (not applicable)           |                 |  |  |  |
| ACR20                             | 37              |  |  |  |
| ACR50                             | 12              |  |  |  |
| ACR70                             | 5.4             |  |  |  |

## Statistical analyses

|                            |                        |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

Analysis Type used was dose escalation.

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 140                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[157]</sup>                   |
| P-value                                 | = 0.589 <sup>[158]</sup>                 |
| Method                                  | Fisher exact                             |
| Parameter estimate                      | Percent difference                       |
| Point estimate                          | 4.7                                      |
| Confidence interval                     |  |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | -12.1                                    |
| upper limit                             | 22                                       |

Notes:

[157] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[158] - ACR50: p-value was calculated using a two-tailed Fisher's exact test-

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 2       |
| Statistical analysis description:       |                              |
| Analysis Type used was dose escalation. |                              |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 141                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[159]</sup>       |
| P-value                                 | = 0.032 <sup>[160]</sup>     |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 20.2                         |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | 2.8                          |
| upper limit                             | 36.7                         |

Notes:

[159] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[160] - ACR50: p-value was calculated using a two-tailed Fisher's exact test-

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 3       |
| Statistical analysis description:       |                              |
| Analysis Type used was dose escalation. |                              |
| Comparison groups                       | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 140                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[161]</sup>       |
| P-value                                 | = 1 <sup>[162]</sup>         |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 0.5                          |



|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -16     |
| upper limit         | 18      |

Notes:

[161] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[162] - ACR50: p-value was calculated using a two-tailed Fisher's exact test-

|   |                               |
|---|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 4        |
| Statistical analysis description:       |                               |
| Analysis Type used was dose escalation. |                               |
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 139                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[163]</sup>        |
| P-value                                 | < 0.001 <sup>[164]</sup>      |
| Method                                  | Fisher exact                  |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | 33.3                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 15.6                          |
| upper limit                             | 48.6                          |

Notes:

[163] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[164] - ACR50: p-value was calculated using a two-tailed Fisher's exact test-

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Statistical Analysis 5                   |
| Statistical analysis description:       |  |
| Analysis Type used was dose escalation. |  |
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 140                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[165]</sup>                   |
| P-value                                 | = 0.212 <sup>[166]</sup>                 |
| Method                                  | Fisher exact                             |
| Parameter estimate                      | Percent difference                       |
| Point estimate                          | 8.9                                      |
| Confidence interval                     |  |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | -3.5                                     |
| upper limit                             | 23.6                                     |

Notes:

[165] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[166] - ACR50: p-value was calculated using a two-tailed Fisher's exact test.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 6 |
|-----------------------------------|------------------------|

|   |                              |
|---|------------------------------|
| Statistical analysis description:       |                              |
| Analysis Type used was dose escalation. |                              |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 141                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[167]</sup>       |
| P-value                                 | = 0.011 <sup>[168]</sup>     |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 18.7                         |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | 4.8                          |
| upper limit                             | 34                           |

Notes:

[167] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[168] - ACR50: p-value was calculated using a two-tailed Fisher's exact test.

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 7       |
| Statistical analysis description:       |                              |
| Analysis Type used was dose escalation. |                              |
| Comparison groups                       | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 140                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[169]</sup>       |
| P-value                                 | = 0.446 <sup>[170]</sup>     |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 4.7                          |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -7                           |
| upper limit                             | 19.1                         |

Notes:

[169] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[170] - ACR50: p-value was calculated using a two-tailed Fisher's exact test.

|   |                               |
|---|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 8        |
| Statistical analysis description:       |                               |
| Analysis Type used was dose escalation. |                               |
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 139                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[171]</sup>        |
| P-value                                 | = 0.003 <sup>[172]</sup>      |
| Method                                  | Fisher exact                  |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | 22.1                          |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 7.6     |
| upper limit         | 37.8    |

Notes:

[171] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[172] - ACR50: p-value was calculated using a two-tailed Fisher's exact test.

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Statistical Analysis 9                   |
| Statistical analysis description:       |  |
| Analysis Type used was dose escalation. |  |
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 140                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[173]</sup>                   |
| P-value                                 | = 1 <sup>[174]</sup>                     |
| Method                                  | Fisher exact                             |
| Parameter estimate                      | Percent difference                       |
| Point estimate                          | -1.3                                     |
| Confidence interval                     |  |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | -8.9                                     |
| upper limit                             | 9.7                                      |

Notes:

[173] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[174] - ACR70: p-value was calculated using a two-tailed Fisher's exact test.

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 10      |
| Statistical analysis description:       |                              |
| Analysis Type used was dose escalation. |                              |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 141                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[175]</sup>       |
| P-value                                 | = 0.317 <sup>[176]</sup>     |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 4.8                          |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -4.1                         |
| upper limit                             | 17.5                         |

Notes:

[175] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[176] - ACR70: p-value was calculated using a two-tailed Fisher's exact test.

|                                   |                         |
|-----------------------------------|-------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 11 |
|-----------------------------------|-------------------------|

Statistical analysis description:

Analysis Type used was dose escalation.

|   |                              |
|---|------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 140                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[177]</sup>       |
| P-value                                 | = 1 <sup>[178]</sup>         |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 0.8                          |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -7.2                         |
| upper limit                             | 12.1                         |

Notes:

[177] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[178] - ACR70: p-value was calculated using a two-tailed Fisher's exact test.

|                                   |                         |
|-----------------------------------|-------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 12 |
|-----------------------------------|-------------------------|

Statistical analysis description:

Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 139                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[179]</sup>        |
| P-value                                 | = 0.106 <sup>[180]</sup>      |
| Method                                  | Fisher exact                  |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | 9.5                           |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -0.5                          |
| upper limit                             | 23.5                          |

Notes:

[179] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[180] - ACR70: p-value was calculated using a two-tailed Fisher's exact test.

### **Secondary: Percentage of Participants who Achieved American College of Rheumatology 20 (ACR20), ACR50 and ACR70 Responses at Day 85 by Region**

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants who Achieved American College of Rheumatology 20 (ACR20), ACR50 and ACR70 Responses at Day 85 by Region |
|-----------------|--|

End point description:

ACR20, ACR50, and ACR70, were defined as  $\geq 20\%$ ,  $\geq 50\%$ , or  $\geq 70\%$  improvement, respectively, in: SJC and TJC and  $\geq 20\%$ ,  $\geq 50\%$ , or  $\geq 70\%$  improvement, respectively, in at least 3 of 5 remaining ACR core measures: participant assessment of pain; participant global assessment of disease activity; physician global assessment of disease activity; self-assessed disability (disability index of the HAQ); and CRP. Data for the European and Japanese regions were reported. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues. Here "n" signifies participants who were evaluable for this measure for the specified region for each arm, respectively.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Day 85               |           |

| End point values                   | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|------------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                 | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed        | 48                                   | 49                    | 48                    | 47                     |
| Units: percentage of participants  |                                      |                       |                       |                        |
| number (not applicable)            |                                      |                       |                       |                        |
| European: ACR20 (n=75,39,41,39,39) | 41                                   | 56.1                  | 41                    | 69.2                   |
| Japanese: ACR20 (n=17,9,8,9,8)     | 44.4                                 | 62.5                  | 22.2                  | 75                     |
| European: ACR50 (n=75,39,41,39,39) | 23.1                                 | 29.3                  | 20.5                  | 30.8                   |
| Japanese: ACR50 (n=17,9,8,9,8)     | 11.1                                 | 37.5                  | 0                     | 50                     |
| European: ACR70 (n=75,39,41,39,39) | 5.1                                  | 9.8                   | 7.7                   | 17.9                   |
| Japanese: ACR70 (n=17,9,8,9,8)     | 0                                    | 12.5                  | 0                     | 0                      |

| End point values                   | Placebo         |  |  |  |
|------------------------------------|-----------------|--|--|--|
| Subject group type                 | Reporting group |  |  |  |
| Number of subjects analysed        | 92              |  |  |  |
| Units: percentage of participants  |                 |  |  |  |
| number (not applicable)            |                 |  |  |  |
| European: ACR20 (n=75,39,41,39,39) | 40              |  |  |  |
| Japanese: ACR20 (n=17,9,8,9,8)     | 23.5            |  |  |  |
| European: ACR50 (n=75,39,41,39,39) | 12              |  |  |  |
| Japanese: ACR50 (n=17,9,8,9,8)     | 11.8            |  |  |  |
| European: ACR70 (n=75,39,41,39,39) | 4               |  |  |  |
| Japanese: ACR70 (n=17,9,8,9,8)     | 11.8            |  |  |  |

## Statistical analyses

| Statistical analysis title              | Statistical Analysis 1                   |
|---|--|
| Statistical analysis description:       |  |
| Analysis Type used was dose escalation. |  |
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 140                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[181]</sup>                   |
| P-value                                 | = 1 <sup>[182]</sup>                     |
| Method                                  | Fisher exact                             |
| Parameter estimate                      | Percent difference                       |
| Point estimate                          | 1  |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -17.7   |
| upper limit         | 20.4    |

Notes:

[181] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[182] - European region: ACR20 - p-value was calculated using a two-tailed Fisher's exact test.

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 2       |
| Statistical analysis description:       |                              |
| Analysis Type used was dose escalation. |                              |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 141                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[183]</sup>       |
| P-value                                 | = 0.12 <sup>[184]</sup>      |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 16.1                         |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -3.1                         |
| upper limit                             | 34.4                         |

Notes:

[183] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001

[184] - European region: ACR20 - p-value was calculated using a two-tailed Fisher's exact test.

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 3       |
| Statistical analysis description:       |                              |
| Analysis Type used was dose escalation. |                              |
| Comparison groups                       | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 140                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[185]</sup>       |
| P-value                                 | = 1 <sup>[186]</sup>         |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 1                            |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -17.7                        |
| upper limit                             | 20.4                         |

Notes:

[185] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[186] - European region: ACR20 - p-value was calculated using a two-tailed Fisher's exact test.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 139                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[187]</sup>        |
| P-value                                 | = 0.005 <sup>[188]</sup>      |
| Method                                  | Fisher exact                  |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | 29.2                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 9.7                           |
| upper limit                             | 46.1                          |

Notes:

[187] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[188] - European region: ACR20 - p-value was calculated using a two-tailed Fisher's exact test.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 5 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis Type used was dose escalation.

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 140                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[189]</sup>                   |
| P-value                                 | = 0.382 <sup>[190]</sup>                 |
| Method                                  | Fisher exact                             |
| Parameter estimate                      | Percent difference                       |
| Point estimate                          | 20.9                                     |
| Confidence interval                     |  |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | -16.4                                    |
| upper limit                             | 55.9                                     |

Notes:

[189] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001

[190] - Japanese region: ACR20 - p-value was calculated using a two-tailed Fisher's exact test.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 6 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis Type used was dose escalation.

|   |                              |
|---|------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 141                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[191]</sup>       |
| P-value                                 | = 0.087 <sup>[192]</sup>     |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 39                           |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -2.7    |
| upper limit         | 69.6    |

Notes:

[191] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[192] - Japanese region: ACR20 - p-value was calculated using a two-tailed Fisher's exact test.

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 7       |
| Statistical analysis description:       |                              |
| Analysis Type used was dose escalation. |                              |
| Comparison groups                       | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 140                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[193]</sup>       |
| P-value                                 | = 1 <sup>[194]</sup>         |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | -1.3                         |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -33.7                        |
| upper limit                             | 35.7                         |

Notes:

[193] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001

[194] - Japanese region: ACR20 - p-value was calculated using a two-tailed Fisher's exact test.

|   |                               |
|---|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 8        |
| Statistical analysis description:       |                               |
| Analysis Type used was dose escalation. |                               |
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 139                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[195]</sup>        |
| P-value                                 | = 0.028 <sup>[196]</sup>      |
| Method                                  | Fisher exact                  |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | 51.5                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 8.2                           |
| upper limit                             | 77                            |

Notes:

[195] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[196] - Japanese region: ACR20 - p-value was calculated using a two-tailed Fisher's exact test.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 9 |
|-----------------------------------|------------------------|



|   |  |
|---|--|
| Statistical analysis description:       |  |
| Analysis Type used was dose escalation. |  |
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 140                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[197]</sup>                   |
| P-value                                 | = 0.175 <sup>[198]</sup>                 |
| Method                                  | Fisher exact                             |
| Parameter estimate                      | Percent difference                       |
| Point estimate                          | 11.1                                     |
| Confidence interval                     |  |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | -2.9                                     |
| upper limit                             | 27.9                                     |

Notes:

[197] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[198] - European region: ACR50 - p-value was calculated using a two-tailed Fisher's exact test.

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 11      |
| Statistical analysis description:       |                              |
| Analysis Type used was dose escalation. |                              |
| Comparison groups                       | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 140                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[199]</sup>       |
| P-value                                 | = 0.271 <sup>[200]</sup>     |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 8.5                          |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -5.1                         |
| upper limit                             | 24.9                         |

Notes:

[199] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[200] - European region: ACR50 - p-value was calculated using a two-tailed Fisher's exact test.

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 10      |
| Statistical analysis description:       |                              |
| Analysis Type used was dose escalation. |                              |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 141                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[201]</sup>       |
| P-value                                 | = 0.026 <sup>[202]</sup>     |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 17.3                         |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 2.4     |
| upper limit         | 34.1    |

Notes:

[201] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[202] - European region: ACR50 - p-value was calculated using a two-tailed Fisher's exact test.

|   |                               |
|---|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 12       |
| Statistical analysis description:       |                               |
| Analysis Type used was dose escalation. |                               |
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 139                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[203]</sup>        |
| P-value                                 | = 0.021 <sup>[204]</sup>      |
| Method                                  | Fisher exact                  |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | 18.8                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 3.4                           |
| upper limit                             | 36                            |

Notes:

[203] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[204] - European region: ACR50 - p-value was calculated using a two-tailed Fisher's exact test.

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 14      |
| Statistical analysis description:       |                              |
| Analysis Type used was dose escalation. |                              |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 141                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[205]</sup>       |
| P-value                                 | = 0.283 <sup>[206]</sup>     |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 25.7                         |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -8.8                         |
| upper limit                             | 63.2                         |

Notes:

[205] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[206] - Japanese region: ACR50 - p-value was calculated using a two-tailed Fisher's exact test.

|                                   |                         |
|-----------------------------------|-------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 13 |
|-----------------------------------|-------------------------|

|   |  |
|---|--|
| Statistical analysis description:       |  |
| Analysis Type used was dose escalation. |  |
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 140                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[207]</sup>                   |
| P-value                                 | = 1 <sup>[208]</sup>                     |
| Method                                  | Fisher exact                             |
| Parameter estimate                      | Percent difference                       |
| Point estimate                          | -0.7                                     |
| Confidence interval                     |  |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | -27                                      |
| upper limit                             | 34.8                                     |

Notes:

[207] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[208] - Japanese region: ACR50 - p-value was calculated using a two-tailed Fisher's exact test.

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 15      |
| Statistical analysis description:       |                              |
| Analysis Type used was dose escalation. |                              |
| Comparison groups                       | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 140                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[209]</sup>       |
| P-value                                 | = 0.529 <sup>[210]</sup>     |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | -11.8                        |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -35                          |
| upper limit                             | 22.7                         |

Notes:

[209] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[210] - Japanese region: ACR50 - p-value was calculated using a two-tailed Fisher's exact test.

|   |                               |
|---|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 16       |
| Statistical analysis description:       |                               |
| Analysis Type used was dose escalation. |                               |
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 139                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[211]</sup>        |
| P-value                                 | = 0.059 <sup>[212]</sup>      |
| Method                                  | Fisher exact                  |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | 38.2                          |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 1.6     |
| upper limit         | 71.2    |

Notes:

[211] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[212] - Japanese region: ACR50 - p-value was calculated using a two-tailed Fisher's exact test.

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Statistical Analysis 17                  |
| Statistical analysis description:       |  |
| Analysis Type used was dose escalation. |  |
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 140                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[213]</sup>                   |
| P-value                                 | = 1 <sup>[214]</sup>                     |
| Method                                  | Fisher exact                             |
| Parameter estimate                      | Percent difference                       |
| Point estimate                          | 1.1                                      |
| Confidence interval                     |  |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | -7                                       |
| upper limit                             | 14.2                                     |

Notes:

[213] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[214] - European region: ACR70 - p-value was calculated using a two-tailed Fisher's exact test.

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 18      |
| Statistical analysis description:       |                              |
| Analysis Type used was dose escalation. |                              |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 141                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[215]</sup>       |
| P-value                                 | = 0.242 <sup>[216]</sup>     |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 5.8                          |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -3.7                         |
| upper limit                             | 19.4                         |

Notes:

[215] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[216] - European region: ACR70 - p-value was calculated using a two-tailed Fisher's exact test.

|                                   |                         |
|-----------------------------------|-------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 19 |
|-----------------------------------|-------------------------|

|   |                              |
|---|------------------------------|
| Statistical analysis description:       |                              |
| Analysis Type used was dose escalation. |                              |
| Comparison groups                       | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 140                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[217]</sup>       |
| P-value                                 | = 0.41 <sup>[218]</sup>      |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 3.7                          |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -5.1                         |
| upper limit                             | 16.9                         |

Notes:

[217] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[218] - European region: ACR70 - p-value was calculated using a two-tailed Fisher's exact test.

|   |                               |
|---|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 20       |
| Statistical analysis description:       |                               |
| Analysis Type used was dose escalation. |                               |
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 139                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[219]</sup>        |
| P-value                                 | = 0.03 <sup>[220]</sup>       |
| Method                                  | Fisher exact                  |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | 13.9                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 2.7                           |
| upper limit                             | 29.5                          |

Notes:

[219] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[220] - European region: ACR70 - p-value was calculated using a two-tailed Fisher's exact test.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Statistical Analysis 21                                       |
| Statistical analysis description:       |   |
| Analysis Type used was dose escalation. |   |
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 188   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other <sup>[221]</sup>  |
| P-value                                 | = 0.529 <sup>[222]</sup>                                      |
| Method                                  | Fisher exact  |
| Parameter estimate                      | Percent difference  |
| Point estimate                          | -11.8   |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -35     |
| upper limit         | 22.7    |

Notes:

[221] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[222] - Japanese region: ACR70 - p-value was calculated using a two-tailed Fisher's exact test.

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 22      |
| Statistical analysis description:       |                              |
| Analysis Type used was dose escalation. |                              |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 141                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[223]</sup>       |
| P-value                                 | = 1 <sup>[224]</sup>         |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 0.7                          |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -26.7                        |
| upper limit                             | 39.5                         |

Notes:

[223] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[224] - Japanese region: ACR70 - p-value was calculated using a two-tailed Fisher's exact test.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Statistical Analysis 23                                       |
| Statistical analysis description:       |   |
| Analysis Type used was dose escalation. |   |
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) v Mavrilimumab 50 mg |
| Number of subjects included in analysis | 188   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | other <sup>[225]</sup>  |
| P-value                                 | = 0.529 <sup>[226]</sup>                                      |
| Method                                  | Fisher exact  |
| Parameter estimate                      | Percent difference  |
| Point estimate                          | -11.8   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -35   |
| upper limit                             | 22.7  |

Notes:

[225] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[226] - Japanese region: ACR70 - p-value was calculated using a two-tailed Fisher's exact test.

|                                   |                         |
|-----------------------------------|-------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 24 |
|-----------------------------------|-------------------------|

Statistical analysis description:

Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 139                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[227]</sup>        |
| P-value                                 | = 1 <sup>[228]</sup>          |
| Method                                  | Fisher exact                  |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | -11.8                         |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -37.5                         |
| upper limit                             | 22.6                          |

Notes:

[227] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

[228] - Japanese region: ACR70 - p-value was calculated using a two-tailed Fisher's exact test.

## Secondary: Number of Participants who Achieved ACR Categorical Responses

|                 |   |
|-----------------|---|
| End point title | Number of Participants who Achieved ACR Categorical Responses |
|-----------------|---|

End point description:

ACR20, ACR50, and ACR70, were defined as  $\geq 20\%$ ,  $\geq 50\%$ , or  $\geq 70\%$  improvement, respectively, in: SJC and TJC and  $\geq 20\%$ ,  $\geq 50\%$ , or  $\geq 70\%$  improvement, respectively, in at least 3 of 5 remaining ACR core measures: participant assessment of pain; participant global assessment of disease activity; physician global assessment of disease activity; self-assessed disability (disability index of the HAQ); and CRP. ACR responses were categorized as "No response", "ACR20 but not ACR50", "ACR50 but not ACR70", and "ACR70". The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues.

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

End point timeframe:

Day 85

| End point values            | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|-----------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type          | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed | 48                                   | 49                    | 48                    | 47                     |
| Units: participants         |                                      |                       |                       |                        |
| No response                 | 28                                   | 21                    | 30                    | 14                     |
| ACR20 but not ACR50         | 10                                   | 13                    | 10                    | 17                     |
| ACR50 but not ACR70         | 8                                    | 10                    | 5                     | 9                      |
| ACR70                       | 2                                    | 5                     | 3                     | 7                      |

|                  |         |  |  |  |
|------------------|---------|--|--|--|
| End point values | Placebo |  |  |  |
|------------------|---------|--|--|--|

|                             |                 |  |  |  |
|-----------------------------|-----------------|--|--|--|
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 92              |  |  |  |
| Units: participants         |                 |  |  |  |
| No response                 | 58              |  |  |  |
| ACR20 but not ACR50         | 23              |  |  |  |
| ACR50 but not ACR70         | 6               |  |  |  |
| ACR70                       | 5               |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Continuous ACR (ACRn) Score

|   |                             |
|---|-----------------------------|
| End point title   | Continuous ACR (ACRn) Score |
| End point description:  |                             |
| ACR score - continuous (ACRn) was defined as the minimum of the percentage improvement in TJC, SJC and the median of the percentage improvements in the other five components of the ACR criteria (participant assessment of pain; participant global assessment of disease activity; physician global assessment of disease activity; disability index of the HAQ; and CRP). Total score range was -100 to 100, where negative numbers indicated worsening and positive numbers indicated improvement. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues. Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure |                             |
| End point type  | Secondary                   |
| End point timeframe:  |                             |
| Day 85  |                             |

| End point values                 | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg   | Mavrilimumab<br>50 mg   | Mavrilimumab<br>100 mg  |
|----------------------------------|--------------------------------------|-------------------------|-------------------------|-------------------------|
| Subject group type               | Reporting group                      | Reporting group         | Reporting group         | Reporting group         |
| Number of subjects analysed      | 44                                   | 47                      | 45                      | 46                      |
| Units: units on a scale          |                                      |                         |                         |                         |
| arithmetic mean (standard error) | 19.13 ( $\pm$<br>5.818)              | 26.31 ( $\pm$<br>5.652) | 12.17 ( $\pm$<br>5.786) | 37.11 ( $\pm$<br>5.723) |

| End point values                 | Placebo            |  |  |  |
|----------------------------------|--------------------|--|--|--|
| Subject group type               | Reporting group    |  |  |  |
| Number of subjects analysed      | 84                 |  |  |  |
| Units: units on a scale          |                    |  |  |  |
| arithmetic mean (standard error) | 5.09 ( $\pm$ 4.23) |  |  |  |



## Statistical analyses

| Statistical analysis title              | Statistical Analysis 1                   |
|---|--|
| Statistical analysis description:       |  |
| Analysis Type used was dose escalation. |  |
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 128                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[229]</sup>                   |
| P-value                                 | = 0.051                                  |
| Method                                  | Repeated measures model                  |
| Parameter estimate                      | Adjusted Mean difference                 |
| Point estimate                          | 14.05                                    |
| Confidence interval                     |  |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | -0.05                                    |
| upper limit                             | 28.15                                    |
| Variability estimate                    | Standard error of the mean               |
| Dispersion value                        | 7.162                                    |

Notes:

[229] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

| Statistical analysis title              | Statistical Analysis 2       |
|---|------------------------------|
| Statistical analysis description:       |                              |
| Analysis Type used was dose escalation. |                              |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 131                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[230]</sup>       |
| P-value                                 | = 0.003                      |
| Method                                  | Repeated measures model      |
| Parameter estimate                      | Adjusted Mean difference     |
| Point estimate                          | 21.23                        |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | 7.39                         |
| upper limit                             | 35.07                        |
| Variability estimate                    | Standard error of the mean   |
| Dispersion value                        | 7.028                        |

Notes:

[230] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

| Statistical analysis title              | Statistical Analysis 3       |
|---|------------------------------|
| Statistical analysis description:       |                              |
| Analysis Type used was dose escalation. |                              |
| Comparison groups                       | Placebo v Mavrilimumab 50 mg |

|   |                            |
|---|----------------------------|
| Number of subjects included in analysis | 129                        |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other <sup>[231]</sup>     |
| P-value                                 | = 0.322                    |
| Method                                  | Repeated measures model    |
| Parameter estimate                      | Adjusted Mean difference   |
| Point estimate                          | 7.09                       |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | -6.96                      |
| upper limit                             | 21.14                      |
| Variability estimate                    | Standard error of the mean |
| Dispersion value                        | 7.136                      |

Notes:

[231] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

|   |                               |
|---|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis 4        |
| Statistical analysis description:       |                               |
| Analysis Type used was dose escalation. |                               |
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 130                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[232]</sup>        |
| P-value                                 | < 0.001                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted Mean difference      |
| Point estimate                          | 32.03                         |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 18.08                         |
| upper limit                             | 45.98                         |
| Variability estimate                    | Standard error of the mean    |
| Dispersion value                        | 7.085                         |

Notes:

[232] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

## Secondary: Continuous ACR (ACRn) Score by Region

|  |                                       |
|--|---------------------------------------|
| End point title  | Continuous ACR (ACRn) Score by Region |
| End point description:   |                                       |
| ACR score - continuous (ACRn) was defined as the minimum of the percentage improvement in TJC, SJC and the median of the percentage improvements in the other five components of the ACR criteria (participant assessment of pain; participant global assessment of disease activity; physician global assessment of disease activity; disability index of the HAQ; and CRP). Total score range was -100 to 100, where negative numbers indicated worsening and positive numbers indicated improvement. Data for European and Japanese regions were reported. The ITT population (Six participants were excluded from the ITT population for data integrity issues). Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure and "n" signifies participants who were evaluable for this measure for the specified region for each arm, respectively. |                                       |
| End point type   | Secondary                             |

End point timeframe:

Day 85

| End point values                   | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|------------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                 | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed        | 44                                   | 47                    | 45                    | 46                     |
| Units: units on a scale            |                                      |                       |                       |                        |
| arithmetic mean (standard error)   |                                      |                       |                       |                        |
| European region (n=69,36,39,38,38) | 19.18 (±<br>6.489)                   | 24.12 (±<br>6.263)    | 12.53 (±<br>6.356)    | 36.06 (±<br>6.356)     |
| Japanese region (n=15,8,8,7,8)     | 18.09 (±<br>13.843)                  | 37.22 (±<br>13.843)   | 10.2 (±<br>14.799)    | 42.09 (±<br>13.843)    |

| End point values                   | Placebo         |  |  |  |
|------------------------------------|-----------------|--|--|--|
| Subject group type                 | Reporting group |  |  |  |
| Number of subjects analysed        | 84              |  |  |  |
| Units: units on a scale            |                 |  |  |  |
| arithmetic mean (standard error)   |                 |  |  |  |
| European region (n=69,36,39,38,38) | 4.71 (± 4.689)  |  |  |  |
| Japanese region (n=15,8,8,7,8)     | 5.99 (± 10.06)  |  |  |  |

## Statistical analyses

| Statistical analysis title   | Statistical Analysis 1                   |
|--|--|
| Statistical analysis description:  |  |
| Analysis reported for European region. Analysis Type used was dose escalation. |  |
| Comparison groups  | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis  | 128                                      |
| Analysis specification   | Pre-specified                            |
| Analysis type  | other <sup>[233]</sup>                   |
| P-value  | = 0.071                                  |
| Method   | Repeated measures model                  |
| Parameter estimate   | Adjusted Mean difference                 |
| Point estimate   | 14.49                                    |
| Confidence interval  |  |
| level  | 95 %                                     |
| sides  | 2-sided                                  |
| lower limit  | -1.24                                    |
| upper limit  | 30.22                                    |
| Variability estimate   | Standard error of the mean               |
| Dispersion value   | 7.981                                    |

Notes:

[233] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

| Statistical analysis title   | Statistical Analysis 2       |
|--|------------------------------|
| Statistical analysis description:  |                              |
| Analysis reported for European region. Analysis Type used was dose escalation. |                              |
| Comparison groups  | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis  | 131                          |
| Analysis specification   | Pre-specified                |
| Analysis type  | other <sup>[234]</sup>       |
| P-value  | = 0.013                      |
| Method   | Repeated measures model      |
| Parameter estimate   | Adjusted mean difference     |
| Point estimate   | 19.43                        |
| Confidence interval  |                              |
| level  | 95 %                         |
| sides  | 2-sided                      |
| lower limit  | 4.06                         |
| upper limit  | 34.8                         |
| Variability estimate   | Standard error of the mean   |
| Dispersion value   | 7.798                        |

Notes:

[234] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

| Statistical analysis title   | Statistical Analysis 3       |
|--|------------------------------|
| Statistical analysis description:  |                              |
| Analysis reported for European region. Analysis Type used was dose escalation. |                              |
| Comparison groups  | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis  | 129                          |
| Analysis specification   | Pre-specified                |
| Analysis type  | other <sup>[235]</sup>       |
| P-value  | = 0.32                       |
| Method   | Repeated measures model      |
| Parameter estimate   | Adjusted mean difference     |
| Point estimate   | 7.84                         |
| Confidence interval  |                              |
| level  | 95 %                         |
| sides  | 2-sided                      |
| lower limit  | -7.68                        |
| upper limit  | 23.36                        |
| Variability estimate   | Standard error of the mean   |
| Dispersion value   | 7.873                        |

Notes:

[235] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

| Statistical analysis title   | Statistical Analysis 4        |
|--|-------------------------------|
| Statistical analysis description:  |                               |
| Analysis reported for European region. Analysis Type used was dose escalation. |                               |
| Comparison groups  | Placebo v Mavrilimumab 100 mg |

|   |                            |
|---|----------------------------|
| Number of subjects included in analysis | 130                        |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other <sup>[236]</sup>     |
| P-value                                 | < 0.001                    |
| Method                                  | Repeated measures model    |
| Parameter estimate                      | Adjusted mean difference   |
| Point estimate                          | 31.37                      |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | 15.85                      |
| upper limit                             | 46.89                      |
| Variability estimate                    | Standard error of the mean |
| Dispersion value                        | 7.873                      |

Notes:

[236] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 5 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis reported for Japanese region. Analysis Type used was dose escalation.

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 128                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[237]</sup>                   |
| P-value                                 | = 0.483                                  |
| Method                                  | Repeated measures model                  |
| Parameter estimate                      | Adjusted mean difference                 |
| Point estimate                          | 12.11                                    |
| Confidence interval                     |  |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | -22.41                                   |
| upper limit                             | 46.64                                    |
| Variability estimate                    | Standard error of the mean               |
| Dispersion value                        | 17.089                                   |

Notes:

[237] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 6 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis reported for Japanese region. Analysis Type used was dose escalation.

|   |                              |
|---|------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 131                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other <sup>[238]</sup>       |
| P-value                                 | = 0.075                      |
| Method                                  | Repeated measures model      |
| Parameter estimate                      | Adjusted mean difference     |
| Point estimate                          | 31.24                        |

|                      |                            |
|----------------------|----------------------------|
| Confidence interval  |                            |
| level                | 95 %                       |
| sides                | 2-sided                    |
| lower limit          | -3.28                      |
| upper limit          | 65.77                      |
| Variability estimate | Standard error of the mean |
| Dispersion value     | 17.089                     |

Notes:

[238] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

|  |                              |
|--|------------------------------|
| <b>Statistical analysis title</b>  | Statistical Analysis 7       |
| Statistical analysis description:  |                              |
| Analysis reported for Japanese region. Analysis Type used was dose escalation. |                              |
| Comparison groups  | Placebo v Mavrilimumab 50 mg |
| Number of subjects included in analysis  | 129                          |
| Analysis specification   | Pre-specified                |
| Analysis type  | other <sup>[239]</sup>       |
| P-value  | = 0.815                      |
| Method   | Repeated measures model      |
| Parameter estimate   | Adjusted mean difference     |
| Point estimate   | 4.22                         |
| Confidence interval  |                              |
| level  | 95 %                         |
| sides  | 2-sided                      |
| lower limit  | -31.89                       |
| upper limit  | 40.32                        |
| Variability estimate   | Standard error of the mean   |
| Dispersion value   | 17.872                       |

Notes:

[239] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

|  |                               |
|--|-------------------------------|
| <b>Statistical analysis title</b>  | Statistical Analysis 8        |
| Statistical analysis description:  |                               |
| Analysis reported for Japanese region. Analysis Type used was dose escalation. |                               |
| Comparison groups  | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis  | 130                           |
| Analysis specification   | Pre-specified                 |
| Analysis type  | other <sup>[240]</sup>        |
| P-value  | = 0.041                       |
| Method   | Repeated measures model       |
| Parameter estimate   | Adjusted mean difference      |
| Point estimate   | 36.11                         |
| Confidence interval  |                               |
| level  | 95 %                          |
| sides  | 2-sided                       |
| lower limit  | 1.58                          |
| upper limit  | 70.63                         |
| Variability estimate   | Standard error of the mean    |
| Dispersion value   | 17.089                        |

Notes:

[240] - 95 percent (%) unconditional exact confidence interval calculated using the method of Agresti and Min, 2001.

## Secondary: Swollen and Tender Joint Count

|                 |                                |
|-----------------|--------------------------------|
| End point title | Swollen and Tender Joint Count |
|-----------------|--------------------------------|

End point description:

Number of swollen joints was determined by examination of 66 joints and identifying when swelling was present. The number of swollen joints was recorded on the joint assessment form, no swelling = 0, swelling = 1. Number of tender joints was determined by examining 68 joints and identified the joints that were painful under pressure or to passive motion. The number of tender joints was recorded on the joint assessment form, no tenderness = 0, tenderness = 1. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues. Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure.

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

End point timeframe:

Day 85

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|--------------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                   | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed          | 45                                   | 47                    | 48                    | 46                     |
| Units: joints                        |                                      |                       |                       |                        |
| arithmetic mean (standard deviation) |                                      |                       |                       |                        |
| Swollen joint count                  | 8 (± 8.4)                            | 5.4 (± 6.8)           | 5.8 (± 7.4)           | 4.4 (± 4.3)            |
| Tender joint count                   | 11.2 (± 10.9)                        | 9.8 (± 10.1)          | 13.9 (± 11.8)         | 9.1 (± 8.8)            |

| End point values                     | Placebo         |  |  |  |
|--------------------------------------|-----------------|--|--|--|
| Subject group type                   | Reporting group |  |  |  |
| Number of subjects analysed          | 85              |  |  |  |
| Units: joints                        |                 |  |  |  |
| arithmetic mean (standard deviation) |                 |  |  |  |
| Swollen joint count                  | 9.2 (± 10)      |  |  |  |
| Tender joint count                   | 14.8 (± 13.1)   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Swollen and Tender Joint Count by Region

|                 |  |
|-----------------|--|
| End point title | Swollen and Tender Joint Count by Region |
|-----------------|--|

End point description:

Number of swollen joints was determined by examination of 66 joints and identifying when swelling was present. The number of swollen joints was recorded on the joint assessment form, no swelling = 0, swelling = 1. Number of tender joints was determined by examining 68 joints and identified the joints

that were painful under pressure or to passive motion. The number of tender joints was recorded on the joint assessment form, no tenderness = 0, tenderness = 1. Data for the European and Japanese regions were reported. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues. Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure and "n" signifies participants who were evaluable for the specified region for each arm, respectively.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Day 85               |           |

| End point values                                    | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|---|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                                  | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed                         | 45                                   | 47                    | 48                    | 46                     |
| Units: joints                                       |                                      |                       |                       |                        |
| arithmetic mean (standard deviation)                |                                      |                       |                       |                        |
| European: Swollen joint count<br>(n=69,36,39,39,38) | 8 (± 8.2)                            | 5.6 (± 7.2)           | 6.4 (± 8)             | 4.2 (± 4.4)            |
| Japanese: Swollen joint count<br>(n=16,9,8,9,8)     | 7.8 (± 9.5)                          | 4.6 (± 4.1)           | 3.1 (± 2.9)           | 4.9 (± 4.3)            |
| European: Tender joint count<br>(n=69,36,39,39,38)  | 11 (± 11.4)                          | 11.2 (± 10.5)         | 14.8 (± 12)           | 9.9 (± 9)              |
| Japanese: Tender joint count<br>(n=16,9,8,9,8)      | 12.1 (± 9.1)                         | 2.8 (± 2.4)           | 9.6 (± 10.1)          | 5.5 (± 7.2)            |

| End point values                                    | Placebo         |  |  |  |
|---|-----------------|--|--|--|
| Subject group type                                  | Reporting group |  |  |  |
| Number of subjects analysed                         | 85              |  |  |  |
| Units: joints                                       |                 |  |  |  |
| arithmetic mean (standard deviation)                |                 |  |  |  |
| European: Swollen joint count<br>(n=69,36,39,39,38) | 9.6 (± 10.4)    |  |  |  |
| Japanese: Swollen joint count<br>(n=16,9,8,9,8)     | 7.6 (± 8)       |  |  |  |
| European: Tender joint count<br>(n=69,36,39,39,38)  | 15.9 (± 13.1)   |  |  |  |
| Japanese: Tender joint count<br>(n=16,9,8,9,8)      | 9.6 (± 11.9)    |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Physician Global Assessment of Disease Activity Score

|                 |   |
|-----------------|---|
| End point title | Physician Global Assessment of Disease Activity Score |
|-----------------|---|



End point description:

Physician Global Assessment of Arthritis was measured on a 0 to 10 centimeter (cm) Visual Analogue Scale (VAS), where 0 cm = very good and 10 cm = very bad. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues. Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure.

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

End point timeframe:

Day 85

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|--------------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                   | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed          | 45                                   | 47                    | 48                    | 46                     |
| Units: cm                            |                                      |                       |                       |                        |
| arithmetic mean (standard deviation) | 3.3 (± 2.16)                         | 3.13 (± 1.8)          | 3.45 (± 1.97)         | 2.95 (± 1.7)           |

| End point values                     | Placebo         |  |  |  |
|--------------------------------------|-----------------|--|--|--|
| Subject group type                   | Reporting group |  |  |  |
| Number of subjects analysed          | 85              |  |  |  |
| Units: cm                            |                 |  |  |  |
| arithmetic mean (standard deviation) | 3.82 (± 2.05)   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Physician Global Assessment of Disease Activity Score by Region

|                 |   |
|-----------------|---|
| End point title | Physician Global Assessment of Disease Activity Score by Region |
|-----------------|---|

End point description:

Physician Global Assessment of Arthritis was measured on a 0 to 10 cm VAS, where 0 cm = very good and 10 cm = very bad. Data for European and Japanese regions were reported. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues. Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure and "n" signifies participants who were evaluable for the specified region for each arm, respectively.

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

End point timeframe:

Day 85

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|--------------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                   | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed          | 45                                   | 47                    | 48                    | 46                     |
| Units: cm                            |                                      |                       |                       |                        |
| arithmetic mean (standard deviation) |                                      |                       |                       |                        |
| European region (n=69,36,39,39,38)   | 3.29 (± 2.21)                        | 3.2 (± 1.79)          | 3.54 (± 1.98)         | 3.12 (± 1.74)          |
| Japanese region (n=16,9,8,9,8)       | 3.37 (± 2.05)                        | 2.79 (± 1.91)         | 3.08 (± 2.03)         | 2.18 (± 1.37)          |

| End point values                     | Placebo         |  |  |  |
|--------------------------------------|-----------------|--|--|--|
| Subject group type                   | Reporting group |  |  |  |
| Number of subjects analysed          | 85              |  |  |  |
| Units: cm                            |                 |  |  |  |
| arithmetic mean (standard deviation) |                 |  |  |  |
| European region (n=69,36,39,39,38)   | 3.93 (± 2.06)   |  |  |  |
| Japanese region (n=16,9,8,9,8)       | 3.31 (± 1.99)   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Patient Global Assessment of Disease Activity Score

|  |   |
|--|---|
| End point title  | Patient Global Assessment of Disease Activity Score |
| End point description:   |   |
| <p>Participants responded to a question, "Considering all the ways your arthritis affects you, how are you feeling today?" by using a 0 - 100 millimeter (mm) VAS, where 0 = very well and 100 = very poorly. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues. Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure.</p> |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| Day 85   |   |

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|--------------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                   | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed          | 45                                   | 47                    | 48                    | 46                     |
| Units: mm                            |                                      |                       |                       |                        |
| arithmetic mean (standard deviation) | 40 (± 22.8)                          | 37.2 (± 21.1)         | 41.1 (± 23.2)         | 35.5 (± 19.3)          |

| End point values                     | Placebo         |  |  |  |
|--------------------------------------|-----------------|--|--|--|
| Subject group type                   | Reporting group |  |  |  |
| Number of subjects analysed          | 85              |  |  |  |
| Units: mm                            |                 |  |  |  |
| arithmetic mean (standard deviation) | 45.1 (± 24.2)   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Patient Global Assessment of Disease Activity Score by Region

|                 |   |
|-----------------|---|
| End point title | Patient Global Assessment of Disease Activity Score by Region |
|-----------------|---|

End point description:

Participants responded to a question, "Considering all the ways your arthritis affects you, how are you feeling today?" by using a 0 - 100 mm VAS, where 0 = very well and 100 = very poorly. Data for European and Japanese regions were reported. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues. Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure and "n" signifies participants who were evaluable for the specified region for each arm, respectively.

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

End point timeframe:

Day 85

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|--------------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                   | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed          | 45                                   | 47                    | 48                    | 46                     |
| Units: mm                            |                                      |                       |                       |                        |
| arithmetic mean (standard deviation) |                                      |                       |                       |                        |
| European region (n=69,36,39,39,38)   | 39.5 (± 22.2)                        | 39 (± 20.6)           | 42.5 (± 23.6)         | 37.3 (± 19.2)          |
| Japanese region (n=16,9,8,9,8)       | 41.9 (± 26.5)                        | 28.8 (± 22.7)         | 35 (± 21.4)           | 26.9 (± 18.7)          |

| End point values                     | Placebo         |  |  |  |
|--------------------------------------|-----------------|--|--|--|
| Subject group type                   | Reporting group |  |  |  |
| Number of subjects analysed          | 85              |  |  |  |
| Units: mm                            |                 |  |  |  |
| arithmetic mean (standard deviation) |                 |  |  |  |
| European region (n=69,36,39,39,38)   | 45.9 (± 23.8)   |  |  |  |
| Japanese region (n=16,9,8,9,8)       | 41.5 (± 26.2)   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Patient Pain Assessment Score

|                 |                               |
|-----------------|-------------------------------|
| End point title | Patient Pain Assessment Score |
|-----------------|-------------------------------|

End point description:

Participants rated the severity of arthritis pain on a 0 to 100 mm VAS, where 0 mm = no pain and 100 mm = most severe pain. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues. Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure.

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

End point timeframe:

Day 85

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|--------------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                   | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed          | 45                                   | 47                    | 48                    | 46                     |
| Units: mm                            |                                      |                       |                       |                        |
| arithmetic mean (standard deviation) | 38.7 (± 24.1)                        | 38.1 (± 24.2)         | 40.1 (± 24.2)         | 34.4 (± 21.6)          |

| End point values                     | Placebo         |  |  |  |
|--------------------------------------|-----------------|--|--|--|
| Subject group type                   | Reporting group |  |  |  |
| Number of subjects analysed          | 85              |  |  |  |
| Units: mm                            |                 |  |  |  |
| arithmetic mean (standard deviation) | 44.5 (± 24.9)   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Patient Pain Assessment Score by Region

|                 |   |
|-----------------|---|
| End point title | Patient Pain Assessment Score by Region |
|-----------------|---|

End point description:

Participants rated the severity of arthritis pain on a 0 to 100 mm VAS, where 0 mm = no pain and 100 mm = most severe pain. Data for European and Japanese regions were reported. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues. Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure and "n" signifies participants who were evaluable for this measure for the specified region for each arm, respectively.

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

End point timeframe:

Day 85

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|--------------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                   | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed          | 45                                   | 47                    | 48                    | 46                     |
| Units: mm                            |                                      |                       |                       |                        |
| arithmetic mean (standard deviation) |                                      |                       |                       |                        |
| European region (n=69,36,39,39,38)   | 38.1 (± 24.1)                        | 39.1 (± 24)           | 41.4 (± 24.4)         | 36 (± 22)              |
| Japanese region (n=16,9,8,9,8)       | 41.1 (± 25.5)                        | 33.3 (± 26.1)         | 34.1 (± 23.6)         | 27 (± 19.4)            |

| End point values                     | Placebo         |  |  |  |
|--------------------------------------|-----------------|--|--|--|
| Subject group type                   | Reporting group |  |  |  |
| Number of subjects analysed          | 85              |  |  |  |
| Units: mm                            |                 |  |  |  |
| arithmetic mean (standard deviation) |                 |  |  |  |
| European region (n=69,36,39,39,38)   | 44.9 (± 24.4)   |  |  |  |
| Japanese region (n=16,9,8,9,8)       | 42.6 (± 27.8)   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Health Assessments Questionnaire-Disability Index (HAQ-DI) Score

|                 |  |
|-----------------|--|
| End point title | Health Assessments Questionnaire-Disability Index (HAQ-DI) Score |
|-----------------|--|

End point description:

HAQ-DI: participant-reported assessment of ability to perform tasks in 8 categories of daily living activities: dress/groom; arise; eat; walk; reach; grip; hygiene; and common activities over past week. Each item scored on 4-point scale from 0 to 3: 0=no difficulty; 1=some difficulty; 2=much difficulty; 3=unable to do. Overall score was computed as the sum of domain scores and divided by the number of domains answered. Total possible score range 0-3 where 0 = least difficulty and 3 = extreme difficulty. The ITT population included all randomized participants. Six participants were excluded from the ITT population for data integrity issues. Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure and "n" signifies participants who were evaluable for this measure for the specified region for each arm, respectively.

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

End point timeframe:

Day 85

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|--------------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                   | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed          | 45                                   | 47                    | 48                    | 46                     |
| Units: units on a scale              |                                      |                       |                       |                        |
| arithmetic mean (standard deviation) | 1.02 (± 0.51)                        | 1.02 (± 0.64)         | 1.1 (± 0.61)          | 0.95 (± 0.59)          |

| End point values                     | Placebo         |  |  |  |
|--------------------------------------|-----------------|--|--|--|
| Subject group type                   | Reporting group |  |  |  |
| Number of subjects analysed          | 85              |  |  |  |
| Units: units on a scale              |                 |  |  |  |
| arithmetic mean (standard deviation) | 1.19 (± 0.68)   |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Health Assessments Questionnaire-Disability Index (HAQ-DI) Score by Region

|                 |   |
|-----------------|---|
| End point title | Health Assessments Questionnaire-Disability Index (HAQ-DI)<br>Score by Region |
|-----------------|---|

End point description:

HAQ-DI: participant-reported assessment of ability to perform tasks in 8 categories of daily living activities: dress/groom; arise; eat; walk; reach; grip; hygiene; and common activities over past week. Each item scored on 4-point scale from 0 to 3: 0=no difficulty; 1=some difficulty; 2=much difficulty; 3=unable to do. Overall score was computed as the sum of domain scores and divided by the number of domains answered. Total possible score range 0-3 where 0 = least difficulty and 3 = extreme difficulty. Data for European and Japanese regions were reported. The ITT population (Six participants were excluded from the ITT population for data integrity issues). Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure and "n" signifies participants who were evaluable for this measure for the specified region for each arm, respectively.

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

End point timeframe:

Day 85

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|--------------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                   | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed          | 45                                   | 47                    | 48                    | 46                     |
| Units: units on a scale              |                                      |                       |                       |                        |
| arithmetic mean (standard deviation) |                                      |                       |                       |                        |
| European region (n=69,36,39,39,38)   | 1.1 (± 0.47)                         | 1.05 (± 0.67)         | 1.16 (± 0.63)         | 1.03 (± 0.56)          |
| Japanese region (n=16,9,8,9,8)       | 0.72 (± 0.61)                        | 0.91 (± 0.53)         | 0.82 (± 0.44)         | 0.56 (± 0.6)           |

| End point values                     | Placebo         |  |  |  |
|--------------------------------------|-----------------|--|--|--|
| Subject group type                   | Reporting group |  |  |  |
| Number of subjects analysed          | 85              |  |  |  |
| Units: units on a scale              |                 |  |  |  |
| arithmetic mean (standard deviation) |                 |  |  |  |
| European region (n=69,36,39,39,38)   | 1.22 (± 0.65)   |  |  |  |
| Japanese region (n=16,9,8,9,8)       | 1.09 (± 0.82)   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Health Assessments Questionnaire (HAQ) Pain Score

|   |   |
|---|---|
| End point title   | Health Assessments Questionnaire (HAQ) Pain Score |
| End point description:  |   |
| Participants were asked to assess the severity of pain in the past week on a 100 VAS with 0 being no pain and 100 being severe pain. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues. Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure. |   |
| End point type  | Secondary   |
| End point timeframe:  |   |
| Day 85  |   |

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|--------------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                   | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed          | 45                                   | 47                    | 48                    | 46                     |
| Units: units on a scale              |                                      |                       |                       |                        |
| arithmetic mean (standard deviation) | 40.9 (± 23.5)                        | 39 (± 25)             | 42.6 (± 23.5)         | 35 (± 20.8)            |

| End point values                     | Placebo         |  |  |  |
|--------------------------------------|-----------------|--|--|--|
| Subject group type                   | Reporting group |  |  |  |
| Number of subjects analysed          | 85              |  |  |  |
| Units: units on a scale              |                 |  |  |  |
| arithmetic mean (standard deviation) | 46.3 (± 24.3)   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Health Assessments Questionnaire (HAQ) Pain Score by Region

|                 |   |
|-----------------|---|
| End point title | Health Assessments Questionnaire (HAQ) Pain Score by Region |
|-----------------|---|

End point description:

Participants were asked to assess the severity of pain in the past week on a 100 VAS with 0 being no pain and 100 being severe pain. Data for European and Japanese regions were reported. The ITT population included all randomized participants. Six participants were excluded from the ITT population for data integrity issues. Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure and "n" signifies participants who were evaluable for this measure for the specified region for each arm, respectively.

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

End point timeframe:

Day 85

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|--------------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                   | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed          | 45                                   | 47                    | 48                    | 46                     |
| Units: units on a scale              |                                      |                       |                       |                        |
| arithmetic mean (standard deviation) |                                      |                       |                       |                        |
| European region (n=69,36,39,39,38)   | 40.3 (± 23.6)                        | 40.6 (± 24.8)         | 43.8 (± 23.8)         | 36.5 (± 21.1)          |
| Japanese region (n=16,9,8,9,8)       | 43.1 (± 24.5)                        | 31 (± 26.1)           | 37.3 (± 22.9)         | 28.3 (± 19.1)          |

| End point values                     | Placebo         |  |  |  |
|--------------------------------------|-----------------|--|--|--|
| Subject group type                   | Reporting group |  |  |  |
| Number of subjects analysed          | 85              |  |  |  |
| Units: units on a scale              |                 |  |  |  |
| arithmetic mean (standard deviation) |                 |  |  |  |
| European region (n=69,36,39,39,38)   | 47 (± 23.9)     |  |  |  |
| Japanese region (n=16,9,8,9,8)       | 43.1 (± 26.3)   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Serum Concentration of C-Reactive Protein (CRP)

|                 |   |
|-----------------|---|
| End point title | Serum Concentration of C-Reactive Protein (CRP) |
|-----------------|---|

End point description:

The test for CRP is a laboratory measurement for evaluation of an acute phase reactant of inflammation through the use of an ultrasensitive assay. A decrease in the level of CRP indicates reduction in inflammation and therefore improvement. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues. Here "N" (number of participants



analyzed) signifies participants who were evaluable for this measure.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Day 85               |           |

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|--------------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                   | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed          | 45                                   | 46                    | 48                    | 46                     |
| Units: mg/L                          |                                      |                       |                       |                        |
| arithmetic mean (standard deviation) | 9.62 ( $\pm$ 4.15)                   | 9.35 ( $\pm$ 3.92)    | 5.71 ( $\pm$ 2.97)    | 6.12 ( $\pm$ 2.9)      |

| End point values                     | Placebo             |  |  |  |
|--------------------------------------|---------------------|--|--|--|
| Subject group type                   | Reporting group     |  |  |  |
| Number of subjects analysed          | 85                  |  |  |  |
| Units: mg/L                          |                     |  |  |  |
| arithmetic mean (standard deviation) | 11.49 ( $\pm$ 4.67) |  |  |  |

## Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|
|----------------------------|------------------------|

Statistical analysis description:

Analysis reported of CRP ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation.

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 130                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[241]</sup>                   |
| P-value                                 | = 0.663                                  |
| Method                                  | Repeated measures model                  |
| Parameter estimate                      | Adjusted GM ratio to Baseline            |
| Point estimate                          | 1.08                                     |
| Confidence interval                     |  |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | 0.77                                     |
| upper limit                             | 1.52                                     |

Notes:

[241] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

| Statistical analysis title | Statistical Type 2 |
|----------------------------|--------------------|
|----------------------------|--------------------|

Statistical analysis description:

Analysis reported of CRP ratio to baseline as Geometric Mean(GM).Analysis Type used was dose

escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg  |
| Number of subjects included in analysis | 131                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[242]</sup>        |
| P-value                                 | = 0.497                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted GM ratio to Baseline |
| Point estimate                          | 0.89                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 0.63                          |
| upper limit                             | 1.25                          |

Notes:

[242] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis reported of CRP ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 50 mg  |
| Number of subjects included in analysis | 133                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[243]</sup>        |
| P-value                                 | = 0.03                        |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted GM Ratio to Baseline |
| Point estimate                          | 0.69                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 0.49                          |
| upper limit                             | 0.96                          |

Notes:

[243] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis reported of CRP ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 131                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[244]</sup>        |
| P-value                                 | = 0.003                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted GM Ratio to Baseline |
| Point estimate                          | 0.6                           |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.43    |
| upper limit         | 0.84    |

Notes:

[244] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

## Secondary: Serum Concentration of C-Reactive Protein (CRP) by Region

|                 |   |
|-----------------|---|
| End point title | Serum Concentration of C-Reactive Protein (CRP) by Region |
|-----------------|---|

End point description:

The test for CRP is a laboratory measurement for evaluation of an acute phase reactant of inflammation through the use of an ultrasensitive assay. A decrease in the level of CRP indicates reduction in inflammation and therefore improvement. Data for European and Japanese regions were reported. The ITT population included all randomized participants. Six participants were excluded from the ITT population for data integrity issues. Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure and "n" signifies participants who were evaluable for this measure for the specified region for each arm, respectively.

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

End point timeframe:

Day 85

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|--------------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                   | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed          | 45                                   | 46                    | 48                    | 46                     |
| Units: mg/L                          |                                      |                       |                       |                        |
| arithmetic mean (standard deviation) |                                      |                       |                       |                        |
| European region (n=69,36,38,39,38)   | 8.86 (± 13.1)                        | 10.24 (± 16.68)       | 6.5 (± 7.6)           | 5.84 (± 9.68)          |
| Japanese region (n=16,9,8,9,8)       | 12.67 (± 18.47)                      | 5.13 (± 6.83)         | 2.28 (± 1.92)         | 7.44 (± 12.26)         |

| End point values                     | Placebo         |  |  |  |
|--------------------------------------|-----------------|--|--|--|
| Subject group type                   | Reporting group |  |  |  |
| Number of subjects analysed          | 85              |  |  |  |
| Units: mg/L                          |                 |  |  |  |
| arithmetic mean (standard deviation) |                 |  |  |  |
| European region (n=69,36,38,39,38)   | 11.89 (± 18.57) |  |  |  |
| Japanese region (n=16,9,8,9,8)       | 9.75 (± 11.93)  |  |  |  |

## Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | Statistical Analysis 1                   |
| Statistical analysis description:   |  |
| European region: Analysis reported of CRP ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation. |  |
| Comparison groups   | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis   | 130                                      |
| Analysis specification  | Pre-specified                            |
| Analysis type   | other <sup>[245]</sup>                   |
| P-value   | = 0.667                                  |
| Method  | Repeated measures model                  |
| Parameter estimate  | Adjusted GM Ratio to Baseline            |
| Point estimate  | 1.09                                     |
| Confidence interval   |  |
| level   | 95 %                                     |
| sides   | 2-sided                                  |
| lower limit   | 0.74                                     |
| upper limit   | 1.6                                      |

Notes:

[245] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|  |                               |
|--|-------------------------------|
| <b>Statistical analysis title</b>  | Statistical Analysis 2        |
| Statistical analysis description:  |                               |
| European region:Analysis reported of CRP ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation. |                               |
| Comparison groups  | Placebo v Mavrilimumab 30 mg  |
| Number of subjects included in analysis  | 131                           |
| Analysis specification   | Pre-specified                 |
| Analysis type  | other <sup>[246]</sup>        |
| P-value  | = 0.966                       |
| Method   | Repeated measures model       |
| Parameter estimate   | Adjusted GM Ratio to Baseline |
| Point estimate   | 1.01                          |
| Confidence interval  |                               |
| level  | 95 %                          |
| sides  | 2-sided                       |
| lower limit  | 0.69                          |
| upper limit  | 1.47                          |

Notes:

[246] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|  |                              |
|--|------------------------------|
| <b>Statistical analysis title</b>  | Statistical Analysis 3       |
| Statistical analysis description:  |                              |
| European region:Analysis reported of CRP ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation. |                              |
| Comparison groups  | Placebo v Mavrilimumab 50 mg |

|   |                               |
|---|-------------------------------|
| Number of subjects included in analysis | 133                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[247]</sup>        |
| P-value                                 | = 0.282                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted GM Ratio to Baseline |
| Point estimate                          | 0.81                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 0.56                          |
| upper limit                             | 1.19                          |

Notes:

[247] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

European region: Analysis reported of CRP ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 131                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[248]</sup>        |
| P-value                                 | = 0.018                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted GM Ratio to Baseline |
| Point estimate                          | 0.63                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 0.43                          |
| upper limit                             | 0.92                          |

Notes:

[248] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 5 |
|-----------------------------------|------------------------|

Statistical analysis description:

Japanese region: Analysis reported of CRP ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation.

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 130                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[249]</sup>                   |
| P-value                                 | = 0.873                                  |
| Method                                  | Repeated measures model                  |
| Parameter estimate                      | Adjusted GM Ratio to Baseline            |
| Point estimate                          | 1.06                                     |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.5     |
| upper limit         | 2.26    |

Notes:

[249] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 6 |
|-----------------------------------|------------------------|

Statistical analysis description:

Japanese region: Analysis reported of CRP ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg  |
| Number of subjects included in analysis | 131                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[250]</sup>        |
| P-value                                 | = 0.093                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted GM Ratio to Baseline |
| Point estimate                          | 0.51                          |

Confidence interval

|             |         |
|-------------|---------|
| level       | 95 %    |
| sides       | 2-sided |
| lower limit | 0.23    |
| upper limit | 1.12    |

Notes:

[250] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 7 |
|-----------------------------------|------------------------|

Statistical analysis description:

Japanese region: Analysis reported of CRP ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 50 mg  |
| Number of subjects included in analysis | 133                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[251]</sup>        |
| P-value                                 | = 0.006                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted GM Ratio to Baseline |
| Point estimate                          | 0.34                          |

Confidence interval

|             |         |
|-------------|---------|
| level       | 95 %    |
| sides       | 2-sided |
| lower limit | 0.16    |
| upper limit | 0.73    |

Notes:

[251] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 8 |
|-----------------------------------|------------------------|

# Statistical analysis description:

Japanese region: Analysis reported of CRP ratio to baseline as Geometric Mean(GM). Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 131                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[252]</sup>        |
| P-value                                 | = 0.072                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted GM Ratio to Baseline |
| Point estimate                          | 0.49                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 0.22                          |
| upper limit                             | 1.07                          |

## Notes:

[252] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

## Secondary: Serum Concentration of Erythrocyte Sedimentation Rate (ESR)

|  |   |
|--|---|
| End point title  | Serum Concentration of Erythrocyte Sedimentation Rate (ESR) |
| End point description:   |   |
| ESR is a laboratory test that provides a non-specific measure of inflammation. The test assesses the rate at which red blood cells fall in a test tube. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues. Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure. |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| Day 85   |   |

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|--------------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                   | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed          | 45                                   | 47                    | 48                    | 46                     |
| Units: mm/hr                         |                                      |                       |                       |                        |
| arithmetic mean (standard deviation) | 31.3 (± 19)                          | 34.1 (± 23.6)         | 29.7 (± 19.1)         | 23.6 (± 14.6)          |

| End point values                     | Placebo         |  |  |  |
|--------------------------------------|-----------------|--|--|--|
| Subject group type                   | Reporting group |  |  |  |
| Number of subjects analysed          | 85              |  |  |  |
| Units: mm/hr                         |                 |  |  |  |
| arithmetic mean (standard deviation) | 34.4 (± 26.5)   |  |  |  |

## Statistical analyses

| Statistical analysis title  | Statistical Analysis 1                   |
|---|--|
| Statistical analysis description:<br>Analysis reported of ESR ratio to baseline as Geometric Mean (GM). Analysis Type used was dose escalation. |  |
| Comparison groups   | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis   | 130                                      |
| Analysis specification  | Pre-specified                            |
| Analysis type   | other <sup>[253]</sup>                   |
| P-value   | = 0.81                                   |
| Method  | Repeated measures model                  |
| Parameter estimate  | Adjusted GM Ratio to Baseline            |
| Point estimate  | 0.97                                     |
| Confidence interval   |  |
| level   | 95 %                                     |
| sides   | 2-sided                                  |
| lower limit   | 0.79                                     |
| upper limit   | 1.2                                      |

Notes:

[253] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

| Statistical analysis title  | Statistical Analysis 2        |
|---|-------------------------------|
| Statistical analysis description:<br>Analysis reported of ESR ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation. |                               |
| Comparison groups   | Placebo v Mavrilimumab 30 mg  |
| Number of subjects included in analysis   | 132                           |
| Analysis specification  | Pre-specified                 |
| Analysis type   | other <sup>[254]</sup>        |
| P-value   | = 0.112                       |
| Method  | Repeated measures model       |
| Parameter estimate  | Adjusted GM Ratio to Baseline |
| Point estimate  | 0.84                          |
| Confidence interval   |                               |
| level   | 95 %                          |
| sides   | 2-sided                       |
| lower limit   | 0.68                          |
| upper limit   | 1.04                          |

Notes:

[254] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

| Statistical analysis title  | Statistical Analysis 3       |
|---|------------------------------|
| Statistical analysis description:<br>Analysis reported of ESR ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation. |                              |
| Comparison groups   | Placebo v Mavrilimumab 50 mg |



|   |                               |
|---|-------------------------------|
| Number of subjects included in analysis | 133                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[255]</sup>        |
| P-value                                 | = 0.01                        |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted GM Ratio to Baseline |
| Point estimate                          | 0.76                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 0.62                          |
| upper limit                             | 0.94                          |

Notes:

[255] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis reported of ESR ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 131                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[256]</sup>        |
| P-value                                 | = 0.002                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted GM Ratio to Baseline |
| Point estimate                          | 0.71                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 0.58                          |
| upper limit                             | 0.88                          |

Notes:

[256] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

## Secondary: Serum Concentration of Erythrocyte Sedimentation Rate (ESR) by Region

|                 |   |
|-----------------|---|
| End point title | Serum Concentration of Erythrocyte Sedimentation Rate (ESR) by Region |
|-----------------|---|

End point description:

ESR is a laboratory test that provides a non-specific measure of inflammation. The test assesses the rate at which red blood cells fall in a test tube. Data for European and Japanese regions were reported. The ITT population included all randomized participants. Six participants were excluded from the ITT population for data integrity issues. Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure and "n" signifies participants who were evaluable for this measure for the specified region for each arm, respectively.

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

End point timeframe:

Day 85

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|--------------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                   | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed          | 45                                   | 47                    | 48                    | 46                     |
| Units: mm/hr                         |                                      |                       |                       |                        |
| arithmetic mean (standard deviation) |                                      |                       |                       |                        |
| European region (n=69,36,39,39,38)   | 30.3 (± 18.3)                        | 33.2 (± 23.9)         | 32.7 (± 19)           | 23.1 (± 14.3)          |
| Japanese region (n=16,9,8,9,8)       | 35 (± 22.5)                          | 38.8 (± 22.6)         | 16.3 (± 13.6)         | 25.9 (± 16.7)          |

| End point values                     | Placebo         |  |  |  |
|--------------------------------------|-----------------|--|--|--|
| Subject group type                   | Reporting group |  |  |  |
| Number of subjects analysed          | 85              |  |  |  |
| Units: mm/hr                         |                 |  |  |  |
| arithmetic mean (standard deviation) |                 |  |  |  |
| European region (n=69,36,39,39,38)   | 33.9 (± 27.8)   |  |  |  |
| Japanese region (n=16,9,8,9,8)       | 36.6 (± 20.8)   |  |  |  |

## Statistical analyses

| Statistical analysis title  | Statistical Analysis 1                   |
|---|--|
| Statistical analysis description:   |  |
| European region: Analysis reported of ESR ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation. |  |
| Comparison groups   | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis   | 130                                      |
| Analysis specification  | Pre-specified                            |
| Analysis type   | other <sup>[257]</sup>                   |
| P-value   | = 0.897                                  |
| Method  | Repeated measures model                  |
| Parameter estimate  | Adjusted GM Ratio to Baseline            |
| Point estimate  | 1.01                                     |
| Confidence interval   |  |
| level   | 95 %                                     |
| sides   | 2-sided                                  |
| lower limit   | 0.81                                     |
| upper limit   | 1.27                                     |

Notes:

[257] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

| Statistical analysis title  | Statistical Analysis 2       |
|---|------------------------------|
| Statistical analysis description:   |                              |
| European region: Analysis reported of ESR ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation. |                              |
| Comparison groups   | Placebo v Mavrilimumab 30 mg |

|   |                               |
|---|-------------------------------|
| Number of subjects included in analysis | 132                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[258]</sup>        |
| P-value                                 | = 0.217                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted GM Ratio to Baseline |
| Point estimate                          | 0.87                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 0.7                           |
| upper limit                             | 1.09                          |

Notes:

[258] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

European region: Analysis reported of ESR ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 50 mg  |
| Number of subjects included in analysis | 133                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[259]</sup>        |
| P-value                                 | = 0.408                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted GM Ratio to Baseline |
| Point estimate                          | 0.91                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 0.73                          |
| upper limit                             | 1.14                          |

Notes:

[259] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

European region:Analysis reported of ESR ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 131                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[260]</sup>        |
| P-value                                 | = 0.009                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted GM Ratio to Baseline |
| Point estimate                          | 0.74                          |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.59    |
| upper limit         | 0.93    |

Notes:

[260] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 5 |
|-----------------------------------|------------------------|

Statistical analysis description:

Japanese region: Analysis reported of ESR ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation.

|   |  |
|---|--|
| Comparison groups                       | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis | 130                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[261]</sup>                   |
| P-value                                 | = 0.474                                  |
| Method                                  | Repeated measures model                  |
| Parameter estimate                      | Adjusted GM Ratio to Baseline            |
| Point estimate                          | 0.83                                     |

Confidence interval

|             |         |
|-------------|---------|
| level       | 95 %    |
| sides       | 2-sided |
| lower limit | 0.49    |
| upper limit | 1.41    |

Notes:

[261] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 6 |
|-----------------------------------|------------------------|

Statistical analysis description:

Japanese region: Analysis reported of ESR ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg  |
| Number of subjects included in analysis | 132                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[262]</sup>        |
| P-value                                 | = 0.352                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted GM Ratio to Baseline |
| Point estimate                          | 0.77                          |

Confidence interval

|             |         |
|-------------|---------|
| level       | 95 %    |
| sides       | 2-sided |
| lower limit | 0.44    |
| upper limit | 1.34    |

Notes:

[262] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 7 |
|-----------------------------------|------------------------|

**Statistical analysis description:**

Japanese region: Analysis reported of ESR ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 50 mg  |
| Number of subjects included in analysis | 133                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[263]</sup>        |
| P-value                                 | < 0.001                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted GM Ratio to Baseline |
| Point estimate                          | 0.4                           |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 0.2                           |
| upper limit                             | 0.58                          |

**Notes:**

[263] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 8 |
|-----------------------------------|------------------------|

**Statistical analysis description:**

Japanese region: Analysis reported of ESR ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 131                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[264]</sup>        |
| P-value                                 | = 0.098                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted GM Ratio to Baseline |
| Point estimate                          | 0.63                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 0.36                          |
| upper limit                             | 1.09                          |

**Notes:**

[264] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

**Secondary: Serum Concentration of Rheumatoid Factor (RF)**

|  |   |
|--|---|
| End point title  | Serum Concentration of Rheumatoid Factor (RF) |
| End point description:   |   |
| The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues. Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure. |   |
| End point type   | Secondary                                     |
| End point timeframe:   |   |
| Day 85   |   |

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg     | Mavrilimumab<br>50 mg   | Mavrilimumab<br>100 mg   |
|--------------------------------------|--------------------------------------|---------------------------|-------------------------|--------------------------|
| Subject group type                   | Reporting group                      | Reporting group           | Reporting group         | Reporting group          |
| Number of subjects analysed          | 45                                   | 46                        | 48                      | 46                       |
| Units: units per milliliter          |                                      |                           |                         |                          |
| arithmetic mean (standard deviation) | 79.62 ( $\pm$<br>93.21)              | 177.84 ( $\pm$<br>352.16) | 85.15 ( $\pm$<br>81.47) | 83.26 ( $\pm$<br>118.14) |

| End point values                     | Placebo                   |  |  |  |
|--------------------------------------|---------------------------|--|--|--|
| Subject group type                   | Reporting group           |  |  |  |
| Number of subjects analysed          | 85                        |  |  |  |
| Units: units per milliliter          |                           |  |  |  |
| arithmetic mean (standard deviation) | 109.82 ( $\pm$<br>135.39) |  |  |  |

## Statistical analyses

| Statistical analysis title  | Statistical Analysis 1                   |
|---|--|
| Statistical analysis description:   |  |
| Analysis reported of RF ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation. |  |
| Comparison groups   | Placebo v Mavrilimumab 10 milligram (mg) |
| Number of subjects included in analysis   | 130                                      |
| Analysis specification  | Pre-specified                            |
| Analysis type   | other <sup>[265]</sup>                   |
| P-value   | = 0.606                                  |
| Method  | Repeated measures model                  |
| Parameter estimate  | Adjusted GM Ratio to Baseline            |
| Point estimate  | 1.03                                     |
| Confidence interval   |  |
| level   | 95 %                                     |
| sides   | 2-sided                                  |
| lower limit   | 0.92                                     |
| upper limit   | 1.16                                     |

Notes:

[265] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

| Statistical analysis title  | Statistical Analysis 2       |
|---|------------------------------|
| Statistical analysis description:   |                              |
| Analysis reported of RF ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation. |                              |
| Comparison groups   | Placebo v Mavrilimumab 30 mg |

|   |                               |
|---|-------------------------------|
| Number of subjects included in analysis | 131                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[266]</sup>        |
| P-value                                 | = 0.902                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted GM Ratio to Baseline |
| Point estimate                          | 1.01                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 0.9                           |
| upper limit                             | 1.13                          |

Notes:

[266] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis reported of RF ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 50 mg  |
| Number of subjects included in analysis | 133                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[267]</sup>        |
| P-value                                 | = 0.391                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted GM Ratio to Baseline |
| Point estimate                          | 1.05                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 0.94                          |
| upper limit                             | 1.18                          |

Notes:

[267] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis reported of RF ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 131                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[268]</sup>        |
| P-value                                 | = 0.554                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted GM Ratio to Baseline |
| Point estimate                          | 1.04                          |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.92    |
| upper limit         | 1.16    |

Notes:

[268] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

## Secondary: Serum Concentration of Anti-Citrullinated-Peptide-Antibody (ACPA)

|                 |   |
|-----------------|---|
| End point title | Serum Concentration of Anti-Citrullinated-Peptide-Antibody (ACPA) |
|-----------------|---|

End point description:

The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues. Here "N" (number of participants analyzed) signifies participants who were evaluable for this measure.

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

End point timeframe:

Day 85

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|--------------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                   | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed          | 45                                   | 46                    | 48                    | 45                     |
| Units: units per milliliter          |                                      |                       |                       |                        |
| arithmetic mean (standard deviation) | 232.22 (±<br>469.86)                 | 211.77 (±<br>250.5)   | 330.82 (±<br>549.05)  | 221.18 (±<br>333.28)   |

| End point values                     | Placebo             |  |  |  |
|--------------------------------------|---------------------|--|--|--|
| Subject group type                   | Reporting group     |  |  |  |
| Number of subjects analysed          | 84                  |  |  |  |
| Units: units per milliliter          |                     |  |  |  |
| arithmetic mean (standard deviation) | 295.9 (±<br>920.92) |  |  |  |

## Statistical analyses

|                            |                        |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

Analysis reported of ACPA ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation.

|                   |  |
|-------------------|--|
| Comparison groups | Placebo v Mavrilimumab 10 milligram (mg) |
|-------------------|--|



|   |                               |
|---|-------------------------------|
| Number of subjects included in analysis | 129                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[269]</sup>        |
| P-value                                 | = 0.286                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted GM Ratio to Baseline |
| Point estimate                          | 0.87                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 0.68                          |
| upper limit                             | 1.12                          |

Notes:

[269] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 2 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis reported of ACPA ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg  |
| Number of subjects included in analysis | 130                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[270]</sup>        |
| P-value                                 | = 0.371                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted GM Ratio to Baseline |
| Point estimate                          | 0.89                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 0.69                          |
| upper limit                             | 1.15                          |

Notes:

[270] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis reported of ACPA ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 50 mg  |
| Number of subjects included in analysis | 132                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[271]</sup>        |
| P-value                                 | = 0.779                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted GM Ratio to Baseline |
| Point estimate                          | 1.04                          |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.81    |
| upper limit         | 1.33    |

Notes:

[271] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical Analysis 4 |
|-----------------------------------|------------------------|

Statistical analysis description:

Analysis reported of ACPA ratio to baseline as Geometric Mean(GM).Analysis Type used was dose escalation.

|   |                               |
|---|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 129                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other <sup>[272]</sup>        |
| P-value                                 | = 0.033                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted GM Ratio to Baseline |
| Point estimate                          | 0.76                          |

Confidence interval

|             |         |
|-------------|---------|
| level       | 95 %    |
| sides       | 2-sided |
| lower limit | 0.59    |
| upper limit | 0.98    |

Notes:

[272] - 95 percent (%) unconditional exact confidence interval was calculated using the method of Agresti and Min, 2001.

## Secondary: Number of Participants who had Additional Medications

|                 |   |
|-----------------|---|
| End point title | Number of Participants who had Additional Medications |
|-----------------|---|

End point description:

Additional medication included concomitant medication (medication used for purposes other than managing rheumatoid arthritis [RA]) and RA medication (for managing RA). Number of participants who used concomitant medication and RA medication was reported by anatomical therapeutic chemical (ATC) classification system. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues.

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

End point timeframe:

Baseline up to Day 169

| End point values                            | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|---|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                          | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed                 | 48                                   | 49                    | 48                    | 47                     |
| Units: participants                         |                                      |                       |                       |                        |
| Concomitant: Blood and blood forming agents | 47                                   | 49                    | 47                    | 45                     |

|   |    |    |    |    |
|---|----|----|----|----|
| Concomitant: Alimentary tract and metabolism        | 25 | 25 | 28 | 23 |
| Concomitant: Cardiovascular system                  | 20 | 19 | 12 | 22 |
| Concomitant: Nervous system                         | 9  | 9  | 6  | 3  |
| Concomitant: Musculo-skeletal system                | 9  | 5  | 8  | 5  |
| Concomitant: Respiratory system                     | 6  | 7  | 5  | 5  |
| Concomitant: Anti-infective for systemic use        | 6  | 6  | 8  | 2  |
| Concomitant: Genito-urinary system and sex hormones | 6  | 6  | 4  | 4  |
| Concomitant: Systemic hormonal preps                | 5  | 4  | 2  | 0  |
| Concomitant: Various                                | 5  | 2  | 2  | 4  |
| Concomitant: Dermatologicals                        | 1  | 5  | 2  | 2  |
| Concomitant: Sensory organs                         | 2  | 3  | 2  | 2  |
| Concomitant: Anti-parasitic products                | 0  | 0  | 0  | 0  |
| RA: Antineoplastic and immunomodulating agents      | 48 | 49 | 48 | 47 |
| RA: Musculo-skeletal system                         | 35 | 38 | 32 | 31 |
| RA: Systemic hormonal preps                         | 23 | 21 | 21 | 23 |
| RA: Nervous system                                  | 0  | 2  | 2  | 1  |
| RA: Alimentary tract and metabolism                 | 2  | 0  | 1  | 0  |
| RA: Dermatologicals                                 | 0  | 0  | 0  | 1  |
| RA: Respiratory system                              | 0  | 0  | 0  | 1  |
| RA: Sensory organs                                  | 0  | 0  | 0  | 1  |

| End point values                                    | Placebo         |  |  |  |
|---|-----------------|--|--|--|
| Subject group type                                  | Reporting group |  |  |  |
| Number of subjects analysed                         | 92              |  |  |  |
| Units: participants                                 |                 |  |  |  |
| Concomitant: Blood and blood forming agents         | 88              |  |  |  |
| Concomitant: Alimentary tract and metabolism        | 45              |  |  |  |
| Concomitant: Cardiovascular system                  | 30              |  |  |  |
| Concomitant: Nervous system                         | 14              |  |  |  |
| Concomitant: Musculo-skeletal system                | 11              |  |  |  |
| Concomitant: Respiratory system                     | 11              |  |  |  |
| Concomitant: Anti-infective for systemic use        | 10              |  |  |  |
| Concomitant: Genito-urinary system and sex hormones | 4               |  |  |  |
| Concomitant: Systemic hormonal preps                | 8               |  |  |  |
| Concomitant: Various                                | 6               |  |  |  |
| Concomitant: Dermatologicals                        | 2               |  |  |  |
| Concomitant: Sensory organs                         | 0               |  |  |  |
| Concomitant: Anti-parasitic products                | 1               |  |  |  |
| RA: Antineoplastic and immunomodulating agents      | 92              |  |  |  |
| RA: Musculo-skeletal system                         | 65              |  |  |  |
| RA: Systemic hormonal preps                         | 47              |  |  |  |
| RA: Nervous system                                  | 4               |  |  |  |
| RA: Alimentary tract and metabolism                 | 0               |  |  |  |

|                        |   |  |  |  |
|------------------------|---|--|--|--|
| RA: Dermatologicals    | 1 |  |  |  |
| RA: Respiratory system | 0 |  |  |  |
| RA: Sensory organs     | 0 |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Change in Methotrexate (MTX) and Corticosteroid (CST) Dose

|   |  |
|---|--|
| End point title   | Number of Participants With Change in Methotrexate (MTX) and Corticosteroid (CST) Dose |
| End point description:  |  |
| <p>Participants received MTX at stable and tolerated dose during baseline were categorized as "low dose (&lt;12.5 mg per week [mg/wk])", "medium dose (<math>\geq</math>12.5 - &lt;20 mg/wk)", and "high dose (<math>\geq</math>20 mg/wk)". Participants received oral CST at stable dose during baseline were categorized as "low dose (&lt;5 mg/day)", and "high dose (<math>\geq</math>5 mg/day)". Change in MTX and CST dose from baseline between Day 1-85 and Day 86-169 were categorized as follows: 'Increased', 'no change' and 'decreased'. Participants were counted once with dose increases counted first, followed by no change and then dose decreases. The ITT population analysis set included all randomized participants regardless of whether participants received any investigational product. Six participants were excluded from the ITT population for data integrity issues. Here "n" signifies participants who were evaluable for the specified parameter for each arm, respectively.</p> |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| Baseline, Day 1 to 85, Day 86 to 169  |  |

| End point values                                  | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|---|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                                | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed                       | 48                                   | 49                    | 48                    | 47                     |
| Units: participants                               |                                      |                       |                       |                        |
| MTX: Low dose (Baseline)<br>(n=92,48,49,48,47)    | 18                                   | 24                    | 29                    | 21                     |
| MTX: Medium dose (Baseline)<br>(n=92,48,49,48,47) | 25                                   | 21                    | 15                    | 25                     |
| MTX: High dose (Baseline)<br>(n=92,48,49,48,47)   | 5                                    | 4                     | 4                     | 1                      |
| MTX: Increased (Day 1-85)<br>(n=92,48,49,48,47)   | 0                                    | 0                     | 0                     | 0                      |
| MTX: No change (Day 1-85)<br>(n=92,48,49,48,47)   | 46                                   | 47                    | 47                    | 45                     |
| MTX: Decreased (Day 1-85)<br>(n=92,48,49,48,47)   | 2                                    | 2                     | 1                     | 2                      |
| MTX: Increased (Day 86-169)<br>(n=85,45,46,48,45) | 3                                    | 3                     | 2                     | 1                      |
| MTX: No change (Day 86-169)<br>(n=85,45,46,48,45) | 42                                   | 42                    | 46                    | 44                     |
| MTX: Decreased (Day 86-169)<br>(n=85,45,46,48,45) | 0                                    | 1                     | 0                     | 0                      |
| CST: Low dose (Baseline)<br>(n=46,22,21,21,23)    | 4                                    | 2                     | 1                     | 1                      |

|   |    |    |    |    |
|---|----|----|----|----|
| CST: High dose (Baseline)<br>(n=46,22,21,21,23)   | 18 | 19 | 20 | 22 |
| CST: Increased (Day 1-85)<br>(n=46,22,21,21,23)   | 0  | 0  | 0  | 0  |
| CST: No change (Day 1-85)<br>(n=46,22,21,21,23)   | 22 | 21 | 21 | 23 |
| CST: Decreased (Day 1-85)<br>(n=46,22,21,21,23)   | 0  | 0  | 0  | 0  |
| CST: Increased (Day 86-169)<br>(n=46,21,21,22,23) | 1  | 2  | 2  | 0  |
| CST: No change (Day 86-169)<br>(n=46,21,21,22,23) | 20 | 19 | 20 | 23 |
| CST: Decreased (Day 86-169)<br>(n=46,21,21,22,23) | 0  | 0  | 0  | 0  |

| End point values                                  | Placebo         |  |  |  |
|---|-----------------|--|--|--|
| Subject group type                                | Reporting group |  |  |  |
| Number of subjects analysed                       | 92              |  |  |  |
| Units: participants                               |                 |  |  |  |
| MTX: Low dose (Baseline)<br>(n=92,48,49,48,47)    | 39              |  |  |  |
| MTX: Medium dose (Baseline)<br>(n=92,48,49,48,47) | 44              |  |  |  |
| MTX: High dose (Baseline)<br>(n=92,48,49,48,47)   | 9               |  |  |  |
| MTX: Increased (Day 1-85)<br>(n=92,48,49,48,47)   | 0               |  |  |  |
| MTX: No change (Day 1-85)<br>(n=92,48,49,48,47)   | 90              |  |  |  |
| MTX: Decreased (Day 1-85)<br>(n=92,48,49,48,47)   | 2               |  |  |  |
| MTX: Increased (Day 86-169)<br>(n=85,45,46,48,45) | 2               |  |  |  |
| MTX: No change (Day 86-169)<br>(n=85,45,46,48,45) | 82              |  |  |  |
| MTX: Decreased (Day 86-169)<br>(n=85,45,46,48,45) | 1               |  |  |  |
| CST: Low dose (Baseline)<br>(n=46,22,21,21,23)    | 6               |  |  |  |
| CST: High dose (Baseline)<br>(n=46,22,21,21,23)   | 40              |  |  |  |
| CST: Increased (Day 1-85)<br>(n=46,22,21,21,23)   | 2               |  |  |  |
| CST: No change (Day 1-85)<br>(n=46,22,21,21,23)   | 44              |  |  |  |
| CST: Decreased (Day 1-85)<br>(n=46,22,21,21,23)   | 0               |  |  |  |
| CST: Increased (Day 86-169)<br>(n=46,21,21,22,23) | 2               |  |  |  |
| CST: No change (Day 86-169)<br>(n=46,21,21,22,23) | 44              |  |  |  |
| CST: Decreased (Day 86-169)<br>(n=46,21,21,22,23) | 0               |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Maximum Observed Serum Concentration (Cmax) for Mavrilimumab After First Dose by Region

|                 |  |
|-----------------|--|
| End point title | Maximum Observed Serum Concentration (Cmax) for Mavrilimumab After First Dose by Region <sup>[273]</sup> |
|-----------------|--|

End point description:

Data for European and Japanese regions were reported. The pharmacokinetic (PK) population included all participants who received mavrilimumab and for whom serum concentrations of mavrilimumab were available for PK data analyses. Here "N" signifies participants who were evaluable for this measure and "n" signifies participants who were evaluable for the specified region for each arm, respectively.

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

End point timeframe:

PK parameters were measured pre-dose on Days 1, 4, 8, 15, 29, 57, and 85 as well as during follow up on Days 88, 99, 113 and 169

Notes:

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

Justification: Placebo-treated participants (N=92) were excluded from pharmacokinetic analysis

| End point values                       | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>100 mg | Mavrilimumab<br>50 mg |
|--|--------------------------------------|-----------------------|------------------------|-----------------------|
| Subject group type                     | Reporting group                      | Reporting group       | Reporting group        | Subject analysis set  |
| Number of subjects analysed            | 46                                   | 49                    | 45                     | 49                    |
| Units: nanogram per milliliter (ng/mL) |                                      |                       |                        |                       |
| geometric mean (standard deviation)    |                                      |                       |                        |                       |
| European region (n=37,41,40,37)        | 128 (± 1130)                         | 917 (± 796)           | 6500 (± 3630)          | 1240 (± 1200)         |
| Japanese region (n=9,8,9,8)            | 61.3 (± 30.3)                        | 633 (± 388)           | 4540 (± 927)           | 1230 (± 652)          |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Reach Maximum Observed Serum Concentration (Tmax) for Mavrilimumab After First Dose by Region

|                 |  |
|-----------------|--|
| End point title | Time to Reach Maximum Observed Serum Concentration (Tmax) for Mavrilimumab After First Dose by Region <sup>[274]</sup> |
|-----------------|--|

End point description:

Data for European and Japanese regions were reported. The PK population included all participants who received mavrilimumab and for whom serum concentrations of mavrilimumab were available for PK data analyses. Here "N" signifies participants who were evaluable for this measure and "n" signifies participants who were evaluable for the specified region for each arm, respectively.

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

End point timeframe:

PK parameters were measured pre-dose on Days 1, 4, 8, 15, 29, 57, and 85 as well as during follow up on Days 88, 99, 113 and 169

Notes:

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

Justification: Placebo-treated participants (N=92) were excluded from pharmacokinetic analysis

| End point values                | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>100 mg | Mavrilimumab<br>50 mg |
|---------------------------------|--------------------------------------|-----------------------|------------------------|-----------------------|
| Subject group type              | Reporting group                      | Reporting group       | Reporting group        | Subject analysis set  |
| Number of subjects analysed     | 46                                   | 49                    | 45                     | 49                    |
| Units: days                     |                                      |                       |                        |                       |
| median (full range (min-max))   |                                      |                       |                        |                       |
| European region (n=37,41,40,37) | 4 (2 to 7)                           | 3 (2 to 12)           | 4 (2 to 8)             | 4 (0 to 8)            |
| Japanese region (n=9,8,9,8)     | 6 (2 to 8)                           | 7 (3 to 9)            | 7 (2 to 8)             | 6 (2 to 9)            |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Area Under the Curve from Time Zero to end of Dosing Interval (AUCtau) for Mavrilimumab After First Dose by Region

|                 |   |
|-----------------|---|
| End point title | Area Under the Curve from Time Zero to end of Dosing Interval (AUCtau) for Mavrilimumab After First Dose by Region <sup>[275]</sup> |
|-----------------|---|

End point description:

Data for European and Japanese regions were reported. The PK population included all participants who received mavrilimumab and for whom serum concentrations of mavrilimumab were available for PK data analyses. Here "N" signifies participants who were evaluable for this measure and "n" signifies participants who were evaluable for the specified region for each arm, respectively.

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

End point timeframe:

PK parameters were measured pre-dose on Days 1, 4, 8, 15, 29, 57, and 85 as well as during follow up on Days 88, 99, 113 and 169

Notes:

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

Justification: Placebo-treated participants (N=92) were excluded from pharmacokinetic analysis

| End point values                                  | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>100 mg | Mavrilimumab<br>50 mg |
|---|--------------------------------------|-----------------------|------------------------|-----------------------|
| Subject group type                                | Reporting group                      | Reporting group       | Reporting group        | Subject analysis set  |
| Number of subjects analysed                       | 46                                   | 49                    | 45                     | 49                    |
| Units: nanogram*day per milliliter<br>(ng*day/mL) |                                      |                       |                        |                       |
| geometric mean (standard deviation)               |                                      |                       |                        |                       |
| European region (n=37,41,40,37)                   | 860 (± 8300)                         | 6330 (± 5320)         | 62500 (± 36600)        | 10200 (± 10800)       |
| Japanese region (n=9,8,9,8)                       | 504 (± 236)                          | 5820 (± 4300)         | 45500 (± 12300)        | 11300 (± 6620)        |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Maximum Observed Serum Concentration (Cmax) for Mavrilimumab

## After Last Dose by Region

|                 |   |
|-----------------|---|
| End point title | Maximum Observed Serum Concentration (Cmax) for Mavrilimumab After Last Dose by Region <sup>[276]</sup> |
|-----------------|---|

### End point description:

Data for European and Japanese regions were reported. The PK population included all participants who received mavrilimumab and for whom serum concentrations of mavrilimumab were available for PK data analyses. Here "N" signifies participants who were evaluable for this measure and "n" signifies participants who were evaluable for the specified region for each arm, respectively.

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

### End point timeframe:

PK parameters were measured pre-dose on Days 1, 4, 8, 15, 29, 57, and 85 as well as during follow up on Days 88, 99, 113 and 169

### Notes:

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

Justification: Placebo-treated participants (N=92) were excluded from pharmacokinetic analysis

| End point values                    | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|-------------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                  | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed         | 42                                   | 40                    | 45                    | 45                     |
| Units: ng/mL                        |                                      |                       |                       |                        |
| geometric mean (standard deviation) |                                      |                       |                       |                        |
| European region (n=33,33,37,37)     | 137 (± 363)                          | 1030 (± 3150)         | 2950 (± 2380)         | 7880 (± 5610)          |
| Japanese region (n=9,7,8,8)         | 136 (± 156)                          | 1200 (± 727)          | 3340 (± 1290)         | 10300 (± 2470)         |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Time to Reach Maximum Observed Serum Concentration (Tmax) for Mavrilimumab After Last Dose by Region

|                 |   |
|-----------------|---|
| End point title | Time to Reach Maximum Observed Serum Concentration (Tmax) for Mavrilimumab After Last Dose by Region <sup>[277]</sup> |
|-----------------|---|

### End point description:

Data for European and Japanese regions were reported. The PK population included all participants who received mavrilimumab and for whom serum concentrations of mavrilimumab were available for PK data analyses. Here "N" signifies participants who were evaluable for this measure and "n" signifies participants who were evaluable for the specified region for each arm, respectively.

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

### End point timeframe:

PK parameters were measured pre-dose on Days 1, 4, 8, 15, 29, 57, and 85 as well as during follow up on Days 88, 99, 113 and 169

### Notes:

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

Justification: Placebo-treated participants (N=92) were excluded from pharmacokinetic analysis



| End point values                | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|---------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type              | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed     | 42                                   | 40                    | 45                    | 45                     |
| Units: days                     |                                      |                       |                       |                        |
| median (full range (min-max))   |                                      |                       |                       |                        |
| European region (n=33,33,37,37) | 3 (0 to 6)                           | 3 (0 to 14)           | 3 (0 to 21)           | 3 (0 to 14)            |
| Japanese region (n=9,7,8,8)     | 3 (1 to 5)                           | 3 (1 to 4)            | 3.5 (0 to 14)         | 2 (0 to 3)             |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Area Under the Curve from Time Zero to end of Dosing Interval (AUCtau) for Mavrilimumab After Last Dose by Region

|                 |  |
|-----------------|--|
| End point title | Area Under the Curve from Time Zero to end of Dosing Interval (AUCtau) for Mavrilimumab After Last Dose by Region <sup>[278]</sup> |
|-----------------|--|

End point description:

Data for European and Japanese regions were reported. The PK population included all participants who received mavrilimumab and for whom serum concentrations of mavrilimumab were available for PK data analyses. Here "N" signifies participants who were evaluable for this measure and "n" signifies participants who were evaluable for the specified region for each arm, respectively.

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

End point timeframe:

PK parameters were measured pre-dose on Days 1, 4, 8, 15, 29, 57, and 85 as well as during follow up on Days 88, 99, 113 and 169

Notes:

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

Justification: Placebo-treated participants (N=92) were excluded from pharmacokinetic analysis

| End point values                    | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|-------------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                  | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed         | 42                                   | 40                    | 45                    | 45                     |
| Units: ng*day/mL                    |                                      |                       |                       |                        |
| geometric mean (standard deviation) |                                      |                       |                       |                        |
| European region (n=33,33,37,37)     | 1060 (± 2770)                        | 9260 (± 26300)        | 27900 (± 26700)       | 80500 (± 64300)        |
| Japanese region (n=9,7,8,8)         | 915 (± 1020)                         | 12100 (± 9150)        | 34900 (± 18000)       | 104000 (± 30300)       |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Terminal Phase Elimination Half-Life (t<sub>1/2</sub>) for Mavrilimumab After Last Dose by Region

|                 |   |
|-----------------|---|
| End point title | Terminal Phase Elimination Half-Life (t1/2) for Mavrilimumab After Last Dose by Region <sup>[279]</sup> |
|-----------------|---|

End point description:

Plasma decay half-life is the time measured for the plasma concentration to decrease by one half. Data for European and Japanese regions were reported. The PK population included all participants who received mavrilimumab and for whom serum concentrations of mavrilimumab were available for PK data analyses. Here "N" signifies participants who were evaluable for this measure and "n" signifies participants who were evaluable for the specified region for each arm, respectively.

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

End point timeframe:

PK parameters were measured pre-dose on Days 1, 4, 8, 15, 29, 57, and 85 as well as during follow up on Days 88, 99, 113 and 169

Notes:

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

Justification: Placebo-treated participants (N=92) were excluded from pharmacokinetic analysis

| End point values                     | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|--------------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                   | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed          | 42                                   | 40                    | 45                    | 45                     |
| Units: days                          |                                      |                       |                       |                        |
| arithmetic mean (standard deviation) |                                      |                       |                       |                        |
| European region (n=33,33,37,37)      | 5.56 (± 4.08)                        | 4.37 (± 2.88)         | 6.33 (± 3.07)         | 6.84 (± 3)             |
| Japanese region (n=9,7,8,8)          | 6.96 (± 4.61)                        | 7.23 (± 5.67)         | 7.38 (± 1.65)         | 7.08 (± 2.19)          |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Accumulation Ratio for Mavrilimumab After Last Dose by Region

|                 |  |
|-----------------|--|
| End point title | Accumulation Ratio for Mavrilimumab After Last Dose by Region <sup>[280]</sup> |
|-----------------|--|

End point description:

Accumulation ratio was calculated as ratio of AUCtau after last dose and AUCtau after first dose. Data for European and Japanese regions were reported. The PK population included all participants who received mavrilimumab and for whom serum concentrations of mavrilimumab were available for PK data analyses. Here "N" signifies participants who were evaluable for this measure and "n" signifies participants who were evaluable for the specified region for each arm, respectively.

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

End point timeframe:

PK parameters were measured pre-dose on Days 1, 4, 8, 15, 29, 57, and 85 as well as during follow up on Days 88, 99, 113 and 169

Notes:

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

Justification: Placebo-treated participants (N=92) were excluded from pharmacokinetic analysis

| End point values                    | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Mavrilimumab<br>50 mg | Mavrilimumab<br>100 mg |
|-------------------------------------|--------------------------------------|-----------------------|-----------------------|------------------------|
| Subject group type                  | Reporting group                      | Reporting group       | Reporting group       | Reporting group        |
| Number of subjects analysed         | 42                                   | 40                    | 45                    | 45                     |
| Units: ratio                        |                                      |                       |                       |                        |
| geometric mean (standard deviation) |                                      |                       |                       |                        |
| European region (n=33,33,37,37)     | 1.22 (± 2.97)                        | 1.36 (± 2.23)         | 2.57 (± 54.1)         | 1.29 (± 0.932)         |
| Japanese region (n=9,7,8,8)         | 1.82 (± 1.85)                        | 1.66 (± 0.716)        | 3.21 (± 3.21)         | 2.28 (± 0.616)         |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants Exhibiting Anti-Drug Antibodies (ADAs) to Mavrilimumab at any Visit

|                 |   |
|-----------------|---|
| End point title | Number of Participants Exhibiting Anti-Drug Antibodies (ADAs) to Mavrilimumab at any Visit <sup>[281]</sup> |
|-----------------|---|

End point description:

ADA detection measured by using electrochemiluminescence assays. The immunogenicity population included all participants who received at least 1 dose of CAM-3001 and for whom at least one serum sample for immunogenicity testing was available.

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

End point timeframe:

Day 1 up to Day 169

Notes:

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

Justification: The subject analysis sets were created for the safety population due to difference in evaluable participants for the reporting groups and data has been represented accordingly; hence not all the baseline period arms included while reporting end point data.

| End point values            | Mavrilimumab<br>10 milligram<br>(mg) | Mavrilimumab<br>30 mg | Placebo              | Mavrilimumab<br>50 mg |
|-----------------------------|--------------------------------------|-----------------------|----------------------|-----------------------|
| Subject group type          | Reporting group                      | Reporting group       | Subject analysis set | Subject analysis set  |
| Number of subjects analysed | 48                                   | 49                    | 96                   | 49                    |
| Units: participants         | 10                                   | 6                     | 3                    | 2                     |

| End point values            | Mavrilimumab<br>100mg |  |  |  |
|-----------------------------|-----------------------|--|--|--|
| Subject group type          | Subject analysis set  |  |  |  |
| Number of subjects analysed | 48                    |  |  |  |
| Units: participants         | 2                     |  |  |  |

## Statistical analyses



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From start of the study drug treatment up to Day 169 (Follow-up)

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 15.0 |
|--------------------|------|

### Reporting groups

|                       |                |
|-----------------------|----------------|
| Reporting group title | CAM-3001 10 MG |
|-----------------------|----------------|

Reporting group description:

Mavrilimumab (CAM-3001) 10 milligram (mg) injection subcutaneously every other week for 12 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) orally or parenterally.

|                       |                |
|-----------------------|----------------|
| Reporting group title | CAM-3001 30 MG |
|-----------------------|----------------|

Reporting group description:

Mavrilimumab (CAM-3001) 30 mg injection subcutaneously every other week for 12 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) orally or parenterally.

|                       |                |
|-----------------------|----------------|
| Reporting group title | CAM-3001 50 MG |
|-----------------------|----------------|

Reporting group description:

Mavrilimumab (CAM-3001) 50 mg injection subcutaneously every other week for 12 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) orally or parenterally.

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | CAM-3001 100 MG |
|-----------------------|-----------------|

Reporting group description:

Mavrilimumab (CAM-3001) 100 mg injection subcutaneously every other week for 12 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) orally or parenterally.

|                       |         |
|-----------------------|---------|
| Reporting group title | PLACEBO |
|-----------------------|---------|

Reporting group description:

Placebo matched to mavrilimumab injection subcutaneously every other week for 12 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) orally or parenterally.

| Serious adverse events                            | CAM-3001 10 MG | CAM-3001 30 MG | CAM-3001 50 MG |
|---|----------------|----------------|----------------|
| Total subjects affected by serious adverse events |                |                |                |
| subjects affected / exposed                       | 2 / 48 (4.17%) | 2 / 49 (4.08%) | 1 / 49 (2.04%) |
| number of deaths (all causes)                     | 0              | 0              | 0              |
| number of deaths resulting from adverse events    | 0              | 0              | 0              |
| Injury, poisoning and procedural complications    |                |                |                |
| Humerus fracture                                  |                |                |                |
| subjects affected / exposed                       | 0 / 48 (0.00%) | 1 / 49 (2.04%) | 0 / 49 (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          |
| Patella fracture                                  |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 48 (0.00%) | 1 / 49 (2.04%) | 0 / 49 (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          |
| Pregnancy, puerperium and perinatal conditions  |                |                |                |
| Abortion spontaneous                            |                |                |                |
| subjects affected / exposed                     | 1 / 48 (2.08%) | 0 / 49 (0.00%) | 0 / 49 (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          |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Intervertebral disc disorder                    |                |                |                |
| subjects affected / exposed                     | 1 / 48 (2.08%) | 0 / 49 (0.00%) | 0 / 49 (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          |
| Rheumatoid arthritis                            |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                |                |                |
| Pneumonia                                       |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

| <b>Serious adverse events</b>                     | CAM-3001 100 MG | PLACEBO        |  |
|---|-----------------|----------------|--|
| Total subjects affected by serious adverse events |                 |                |  |
| subjects affected / exposed                       | 0 / 48 (0.00%)  | 1 / 96 (1.04%) |  |
| number of deaths (all causes)                     | 0               | 0              |  |
| number of deaths resulting from adverse events    | 0               | 0              |  |
| Injury, poisoning and procedural complications    |                 |                |  |
| Humerus fracture                                  |                 |                |  |
| subjects affected / exposed                       | 0 / 48 (0.00%)  | 0 / 96 (0.00%) |  |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0          |  |
| Patella fracture                                  |                 |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pregnancy, puerperium and perinatal conditions  |                |                |  |
| Abortion spontaneous                            |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Musculoskeletal and connective tissue disorders |                |                |  |
| Intervertebral disc disorder                    |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Rheumatoid arthritis                            |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Infections and infestations                     |                |                |  |
| Pneumonia                                       |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

Frequency threshold for reporting non-serious adverse events: 0 %

| <b>Non-serious adverse events</b>                     | CAM-3001 10 MG   | CAM-3001 30 MG   | CAM-3001 50 MG   |
|---|------------------|------------------|------------------|
| Total subjects affected by non-serious adverse events |                  |                  |                  |
| subjects affected / exposed                           | 32 / 48 (66.67%) | 29 / 49 (59.18%) | 26 / 49 (53.06%) |
| Vascular disorders                                    |                  |                  |                  |
| Hypertension  |                  |                  |                  |
| subjects affected / exposed                           | 0 / 48 (0.00%)   | 1 / 49 (2.04%)   | 0 / 49 (0.00%)   |
| occurrences (all)                                     | 0                | 1                | 0                |
| Venous insufficiency                                  |                  |                  |                  |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)        | 0 / 48 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 | 1 / 49 (2.04%)<br>1 |
| General disorders and administration<br>site conditions |                     |                     |                     |
| Asthenia  |                     |                     |                     |
| subjects affected / exposed                             | 0 / 48 (0.00%)      | 1 / 49 (2.04%)      | 0 / 49 (0.00%)      |
| occurrences (all)                                       | 0                   | 1                   | 0                   |
| Fatigue   |                     |                     |                     |
| subjects affected / exposed                             | 0 / 48 (0.00%)      | 1 / 49 (2.04%)      | 0 / 49 (0.00%)      |
| occurrences (all)                                       | 0                   | 1                   | 0                   |
| Injection site pain                                     |                     |                     |                     |
| subjects affected / exposed                             | 0 / 48 (0.00%)      | 1 / 49 (2.04%)      | 0 / 49 (0.00%)      |
| occurrences (all)                                       | 0                   | 2                   | 0                   |
| Injection site papule                                   |                     |                     |                     |
| subjects affected / exposed                             | 0 / 48 (0.00%)      | 1 / 49 (2.04%)      | 0 / 49 (0.00%)      |
| occurrences (all)                                       | 0                   | 1                   | 0                   |
| Malaise   |                     |                     |                     |
| subjects affected / exposed                             | 0 / 48 (0.00%)      | 0 / 49 (0.00%)      | 0 / 49 (0.00%)      |
| occurrences (all)                                       | 0                   | 0                   | 0                   |
| Pyrexia   |                     |                     |                     |
| subjects affected / exposed                             | 0 / 48 (0.00%)      | 0 / 49 (0.00%)      | 2 / 49 (4.08%)      |
| occurrences (all)                                       | 0                   | 0                   | 2                   |
| Immune system disorders                                 |                     |                     |                     |
| Hypersensitivity  |                     |                     |                     |
| subjects affected / exposed                             | 0 / 48 (0.00%)      | 1 / 49 (2.04%)      | 1 / 49 (2.04%)      |
| occurrences (all)                                       | 0                   | 1                   | 1                   |
| Social circumstances                                    |                     |                     |                     |
| Family stress   |                     |                     |                     |
| subjects affected / exposed                             | 0 / 48 (0.00%)      | 0 / 49 (0.00%)      | 0 / 49 (0.00%)      |
| occurrences (all)                                       | 0                   | 0                   | 0                   |
| Reproductive system and breast<br>disorders             |                     |                     |                     |
| Amenorrhoea   |                     |                     |                     |
| subjects affected / exposed                             | 1 / 48 (2.08%)      | 0 / 49 (0.00%)      | 0 / 49 (0.00%)      |
| occurrences (all)                                       | 1                   | 0                   | 0                   |
| Breast cyst   |                     |                     |                     |
| subjects affected / exposed                             | 0 / 48 (0.00%)      | 0 / 49 (0.00%)      | 0 / 49 (0.00%)      |
| occurrences (all)                                       | 0                   | 0                   | 0                   |



|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| Menopausal symptoms<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 48 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 |
| Metrorrhagia<br>subjects affected / exposed<br>occurrences (all)                         | 1 / 48 (2.08%)<br>3 | 0 / 49 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal disorders  |                     |                     |                     |
| Cough<br>subjects affected / exposed<br>occurrences (all)                                | 1 / 48 (2.08%)<br>1 | 0 / 49 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)                             | 1 / 48 (2.08%)<br>1 | 0 / 49 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)                            | 1 / 48 (2.08%)<br>1 | 0 / 49 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 |
| Nasal inflammation<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 48 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 |
| Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 48 (0.00%)<br>0 | 1 / 49 (2.04%)<br>1 | 0 / 49 (0.00%)<br>0 |
| Upper respiratory tract inflammation<br>subjects affected / exposed<br>occurrences (all) | 0 / 48 (0.00%)<br>0 | 1 / 49 (2.04%)<br>1 | 0 / 49 (0.00%)<br>0 |
| Psychiatric disorders  |                     |                     |                     |
| Acute stress disorder<br>subjects affected / exposed<br>occurrences (all)                | 0 / 48 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 |
| Depression<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 48 (0.00%)<br>0 | 1 / 49 (2.04%)<br>1 | 0 / 49 (0.00%)<br>0 |
| Sleep disorder<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 48 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 |
| Investigations   |                     |                     |                     |

|  |                  |                |                 |
|--|------------------|----------------|-----------------|
| Alanine aminotransferase increased           |                  |                |                 |
| subjects affected / exposed                  | 1 / 48 (2.08%)   | 2 / 49 (4.08%) | 1 / 49 (2.04%)  |
| occurrences (all)                            | 1                | 2              | 1               |
| Aspartate aminotransferase increased         |                  |                |                 |
| subjects affected / exposed                  | 0 / 48 (0.00%)   | 0 / 49 (0.00%) | 1 / 49 (2.04%)  |
| occurrences (all)                            | 0                | 0              | 1               |
| Blood cholesterol increased                  |                  |                |                 |
| subjects affected / exposed                  | 0 / 48 (0.00%)   | 0 / 49 (0.00%) | 1 / 49 (2.04%)  |
| occurrences (all)                            | 0                | 0              | 1               |
| Blood triglycerides increased                |                  |                |                 |
| subjects affected / exposed                  | 0 / 48 (0.00%)   | 0 / 49 (0.00%) | 0 / 49 (0.00%)  |
| occurrences (all)                            | 0                | 0              | 0               |
| Blood urine present                          |                  |                |                 |
| subjects affected / exposed                  | 0 / 48 (0.00%)   | 0 / 49 (0.00%) | 0 / 49 (0.00%)  |
| occurrences (all)                            | 0                | 0              | 0               |
| Carbon monoxide diffusing capacity decreased |                  |                |                 |
| subjects affected / exposed                  | 10 / 48 (20.83%) | 3 / 49 (6.12%) | 5 / 49 (10.20%) |
| occurrences (all)                            | 13               | 3              | 5               |
| Eosinophil count increased                   |                  |                |                 |
| subjects affected / exposed                  | 1 / 48 (2.08%)   | 0 / 49 (0.00%) | 0 / 49 (0.00%)  |
| occurrences (all)                            | 1                | 0              | 0               |
| Forced expiratory volume decreased           |                  |                |                 |
| subjects affected / exposed                  | 0 / 48 (0.00%)   | 0 / 49 (0.00%) | 1 / 49 (2.04%)  |
| occurrences (all)                            | 0                | 0              | 1               |
| Gamma-glutamyltransferase increased          |                  |                |                 |
| subjects affected / exposed                  | 0 / 48 (0.00%)   | 0 / 49 (0.00%) | 0 / 49 (0.00%)  |
| occurrences (all)                            | 0                | 0              | 0               |
| Hepatic enzyme increased                     |                  |                |                 |
| subjects affected / exposed                  | 1 / 48 (2.08%)   | 0 / 49 (0.00%) | 0 / 49 (0.00%)  |
| occurrences (all)                            | 1                | 0              | 0               |
| Nitrite urine                                |                  |                |                 |
| subjects affected / exposed                  | 0 / 48 (0.00%)   | 0 / 49 (0.00%) | 1 / 49 (2.04%)  |
| occurrences (all)                            | 0                | 0              | 1               |
| Spirometry abnormal                          |                  |                |                 |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)  | 1 / 48 (2.08%)<br>1 | 0 / 49 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 |
| Transaminases increased<br>subjects affected / exposed<br>occurrences (all)                     | 3 / 48 (6.25%)<br>4 | 1 / 49 (2.04%)<br>2 | 1 / 49 (2.04%)<br>1 |
| Urine albumin/creatinine ratio<br>increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 48 (0.00%)<br>0 | 1 / 49 (2.04%)<br>1 | 0 / 49 (0.00%)<br>0 |
| Injury, poisoning and procedural<br>complications   |                     |                     |                     |
| Ankle fracture<br>subjects affected / exposed<br>occurrences (all)                              | 1 / 48 (2.08%)<br>1 | 0 / 49 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 |
| Arthropod bite<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 48 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 |
| Contusion<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 48 (0.00%)<br>0 | 1 / 49 (2.04%)<br>1 | 0 / 49 (0.00%)<br>0 |
| Excoriation<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 48 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 |
| Foot fracture<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 48 (0.00%)<br>0 | 1 / 49 (2.04%)<br>1 | 0 / 49 (0.00%)<br>0 |
| Joint injury<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 48 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 |
| Toxicity to various agents<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 48 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 | 1 / 49 (2.04%)<br>1 |
| Cardiac disorders   |                     |                     |                     |
| Aortic valve incompetence<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 48 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 |
| Arteriosclerosis coronary artery  |                     |                     |                     |

|                                      |                |                |                |
|--------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Cardiac hypertrophy                  |                |                |                |
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Ventricular extrasystoles            |                |                |                |
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Atrioventricular block first degree  |                |                |                |
| subjects affected / exposed          | 0 / 48 (0.00%) | 1 / 49 (2.04%) | 0 / 49 (0.00%) |
| occurrences (all)                    | 0              | 1              | 0              |
| Palpitations                         |                |                |                |
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Supraventricular extrasystoles       |                |                |                |
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Nervous system disorders             |                |                |                |
| Autonomic nervous system imbalance   |                |                |                |
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all)                    | 0              | 0              | 1              |
| Head discomfort                      |                |                |                |
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Headache                             |                |                |                |
| subjects affected / exposed          | 1 / 48 (2.08%) | 0 / 49 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all)                    | 1              | 0              | 1              |
| Hypoaesthesia                        |                |                |                |
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0              |
| Blood and lymphatic system disorders |                |                |                |
| Anaemia                              |                |                |                |
| subjects affected / exposed          | 2 / 48 (4.17%) | 0 / 49 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all)                    | 2              | 0              | 1              |
| Eosinophilia                         |                |                |                |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Leukopenia                  |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 49 (2.04%) | 0 / 49 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Lymphopenia                 |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Monocytopenia               |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Monocytosis                 |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Neutropenia                 |                |                |                |
| subjects affected / exposed | 1 / 48 (2.08%) | 2 / 49 (4.08%) | 2 / 49 (4.08%) |
| occurrences (all)           | 2              | 2              | 2              |
| Thrombocytopenia            |                |                |                |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Thrombocytosis              |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Ear and labyrinth disorders |                |                |                |
| Ear discomfort              |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Vertigo                     |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Eye disorders               |                |                |                |
| Dry eye                     |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all)           | 0              | 0              | 1              |
| Scleritis                   |                |                |                |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 48 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 | 0 / 49 (0.00%)<br>0 |
| Gastrointestinal disorders                       |                     |                     |                     |
| Diarrhoea  |                     |                     |                     |
| subjects affected / exposed                      | 0 / 48 (0.00%)      | 1 / 49 (2.04%)      | 0 / 49 (0.00%)      |
| occurrences (all)                                | 0                   | 1                   | 0                   |
| Dry mouth  |                     |                     |                     |
| subjects affected / exposed                      | 1 / 48 (2.08%)      | 0 / 49 (0.00%)      | 0 / 49 (0.00%)      |
| occurrences (all)                                | 1                   | 0                   | 0                   |
| Flatulence                                       |                     |                     |                     |
| subjects affected / exposed                      | 1 / 48 (2.08%)      | 0 / 49 (0.00%)      | 0 / 49 (0.00%)      |
| occurrences (all)                                | 1                   | 0                   | 0                   |
| Gastritis  |                     |                     |                     |
| subjects affected / exposed                      | 1 / 48 (2.08%)      | 1 / 49 (2.04%)      | 0 / 49 (0.00%)      |
| occurrences (all)                                | 1                   | 1                   | 0                   |
| Nausea   |                     |                     |                     |
| subjects affected / exposed                      | 0 / 48 (0.00%)      | 0 / 49 (0.00%)      | 0 / 49 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Abdominal pain upper                             |                     |                     |                     |
| subjects affected / exposed                      | 0 / 48 (0.00%)      | 0 / 49 (0.00%)      | 0 / 49 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Enterocolitis                                    |                     |                     |                     |
| subjects affected / exposed                      | 0 / 48 (0.00%)      | 0 / 49 (0.00%)      | 0 / 49 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Gastrooesophageal reflux disease                 |                     |                     |                     |
| subjects affected / exposed                      | 1 / 48 (2.08%)      | 0 / 49 (0.00%)      | 0 / 49 (0.00%)      |
| occurrences (all)                                | 1                   | 0                   | 0                   |
| Tooth malformation                               |                     |                     |                     |
| subjects affected / exposed                      | 0 / 48 (0.00%)      | 0 / 49 (0.00%)      | 1 / 49 (2.04%)      |
| occurrences (all)                                | 0                   | 0                   | 1                   |
| Toothache  |                     |                     |                     |
| subjects affected / exposed                      | 1 / 48 (2.08%)      | 0 / 49 (0.00%)      | 0 / 49 (0.00%)      |
| occurrences (all)                                | 1                   | 0                   | 0                   |
| Vomiting   |                     |                     |                     |
| subjects affected / exposed                      | 0 / 48 (0.00%)      | 0 / 49 (0.00%)      | 0 / 49 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |

|  |                |                |                |
|--|----------------|----------------|----------------|
| Hepatobiliary disorders                |                |                |                |
| Hepatic function abnormal              |                |                |                |
| subjects affected / exposed            | 1 / 48 (2.08%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)                      | 1              | 0              | 0              |
| Skin and subcutaneous tissue disorders |                |                |                |
| Alopecia                               |                |                |                |
| subjects affected / exposed            | 1 / 48 (2.08%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)                      | 1              | 0              | 0              |
| Dermatitis                             |                |                |                |
| subjects affected / exposed            | 0 / 48 (0.00%) | 1 / 49 (2.04%) | 0 / 49 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0              |
| Eczema                                 |                |                |                |
| subjects affected / exposed            | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Eczema asteatotic                      |                |                |                |
| subjects affected / exposed            | 0 / 48 (0.00%) | 1 / 49 (2.04%) | 0 / 49 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0              |
| Haemorrhage subcutaneous               |                |                |                |
| subjects affected / exposed            | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all)                      | 0              | 0              | 1              |
| Papule                                 |                |                |                |
| subjects affected / exposed            | 1 / 48 (2.08%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)                      | 1              | 0              | 0              |
| Pruritus                               |                |                |                |
| subjects affected / exposed            | 0 / 48 (0.00%) | 1 / 49 (2.04%) | 0 / 49 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0              |
| Rash                                   |                |                |                |
| subjects affected / exposed            | 0 / 48 (0.00%) | 1 / 49 (2.04%) | 0 / 49 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0              |
| Rash maculo-papular                    |                |                |                |
| subjects affected / exposed            | 1 / 48 (2.08%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)                      | 1              | 0              | 0              |
| Skin exfoliation                       |                |                |                |
| subjects affected / exposed            | 1 / 48 (2.08%) | 0 / 49 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all)                      | 1              | 0              | 1              |
| Spider naevus                          |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Urticaria                                       |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Urticaria papular                               |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Renal and urinary disorders                     |                |                |                |
| Haematuria                                      |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Ketonuria                                       |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 1 / 49 (2.04%) | 0 / 49 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0              |
| Proteinuria                                     |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 1 / 49 (2.04%) | 0 / 49 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0              |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Lumbar spinal stenosis                          |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 1 / 49 (2.04%) | 0 / 49 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0              |
| Bursitis  |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Muscle spasms                                   |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Musculoskeletal pain                            |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Myalgia   |                |                |                |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 1 / 49 (2.04%) | 0 / 49 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0              |
| Neck pain                                       |                |                |                |



|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Osteoarthritis              |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all)           | 0              | 0              | 1              |
| Osteoporosis                |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Rheumatoid arthritis        |                |                |                |
| subjects affected / exposed | 3 / 48 (6.25%) | 2 / 49 (4.08%) | 3 / 49 (6.12%) |
| occurrences (all)           | 3              | 2              | 5              |
| Rotator cuff syndrome       |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 49 (2.04%) | 0 / 49 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Spinal osteoarthritis       |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Infections and infestations |                |                |                |
| Acute tonsillitis           |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Adenoiditis                 |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Bronchitis                  |                |                |                |
| subjects affected / exposed | 1 / 48 (2.08%) | 1 / 49 (2.04%) | 0 / 49 (0.00%) |
| occurrences (all)           | 1              | 1              | 0              |
| Bronchitis viral            |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Cellulitis                  |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Cystitis                    |                |                |                |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |

|                                  |                |                 |                |
|----------------------------------|----------------|-----------------|----------------|
| Enteritis infectious             |                |                 |                |
| subjects affected / exposed      | 0 / 48 (0.00%) | 0 / 49 (0.00%)  | 0 / 49 (0.00%) |
| occurrences (all)                | 0              | 0               | 0              |
| Erysipelas                       |                |                 |                |
| subjects affected / exposed      | 0 / 48 (0.00%) | 1 / 49 (2.04%)  | 0 / 49 (0.00%) |
| occurrences (all)                | 0              | 1               | 0              |
| Gastrointestinal infection       |                |                 |                |
| subjects affected / exposed      | 0 / 48 (0.00%) | 0 / 49 (0.00%)  | 1 / 49 (2.04%) |
| occurrences (all)                | 0              | 0               | 1              |
| Gastrointestinal viral infection |                |                 |                |
| subjects affected / exposed      | 0 / 48 (0.00%) | 0 / 49 (0.00%)  | 0 / 49 (0.00%) |
| occurrences (all)                | 0              | 0               | 0              |
| Genitourinary tract infection    |                |                 |                |
| subjects affected / exposed      | 0 / 48 (0.00%) | 0 / 49 (0.00%)  | 0 / 49 (0.00%) |
| occurrences (all)                | 0              | 0               | 0              |
| Herpangina                       |                |                 |                |
| subjects affected / exposed      | 0 / 48 (0.00%) | 0 / 49 (0.00%)  | 0 / 49 (0.00%) |
| occurrences (all)                | 0              | 0               | 0              |
| Herpes zoster                    |                |                 |                |
| subjects affected / exposed      | 0 / 48 (0.00%) | 0 / 49 (0.00%)  | 0 / 49 (0.00%) |
| occurrences (all)                | 0              | 0               | 0              |
| Infected bites                   |                |                 |                |
| subjects affected / exposed      | 0 / 48 (0.00%) | 0 / 49 (0.00%)  | 0 / 49 (0.00%) |
| occurrences (all)                | 0              | 0               | 0              |
| Influenza                        |                |                 |                |
| subjects affected / exposed      | 2 / 48 (4.17%) | 1 / 49 (2.04%)  | 2 / 49 (4.08%) |
| occurrences (all)                | 2              | 1               | 2              |
| Nasopharyngitis                  |                |                 |                |
| subjects affected / exposed      | 2 / 48 (4.17%) | 5 / 49 (10.20%) | 3 / 49 (6.12%) |
| occurrences (all)                | 2              | 7               | 3              |
| Oral herpes                      |                |                 |                |
| subjects affected / exposed      | 1 / 48 (2.08%) | 2 / 49 (4.08%)  | 0 / 49 (0.00%) |
| occurrences (all)                | 1              | 2               | 0              |
| Pharyngitis                      |                |                 |                |
| subjects affected / exposed      | 0 / 48 (0.00%) | 1 / 49 (2.04%)  | 2 / 49 (4.08%) |
| occurrences (all)                | 0              | 1               | 2              |

|                                   |                |                |                |
|-----------------------------------|----------------|----------------|----------------|
| Pyelonephritis                    |                |                |                |
| subjects affected / exposed       | 0 / 48 (0.00%) | 1 / 49 (2.04%) | 0 / 49 (0.00%) |
| occurrences (all)                 | 0              | 1              | 0              |
| Respiratory tract infection       |                |                |                |
| subjects affected / exposed       | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Respiratory tract infection viral |                |                |                |
| subjects affected / exposed       | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all)                 | 0              | 0              | 1              |
| Rhinitis                          |                |                |                |
| subjects affected / exposed       | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all)                 | 0              | 0              | 1              |
| Sinusitis                         |                |                |                |
| subjects affected / exposed       | 0 / 48 (0.00%) | 1 / 49 (2.04%) | 0 / 49 (0.00%) |
| occurrences (all)                 | 0              | 1              | 0              |
| Streptococcal infection           |                |                |                |
| subjects affected / exposed       | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Tinea pedis                       |                |                |                |
| subjects affected / exposed       | 1 / 48 (2.08%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)                 | 1              | 0              | 0              |
| Tinea versicolour                 |                |                |                |
| subjects affected / exposed       | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all)                 | 0              | 0              | 1              |
| Tonsillitis                       |                |                |                |
| subjects affected / exposed       | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all)                 | 0              | 0              | 1              |
| Upper respiratory tract infection |                |                |                |
| subjects affected / exposed       | 2 / 48 (4.17%) | 1 / 49 (2.04%) | 2 / 49 (4.08%) |
| occurrences (all)                 | 2              | 1              | 2              |
| Urinary tract infection           |                |                |                |
| subjects affected / exposed       | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Viral infection                   |                |                |                |
| subjects affected / exposed       | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |

|                                    |                |                |                |
|------------------------------------|----------------|----------------|----------------|
| Metabolism and nutrition disorders |                |                |                |
| Diabetes mellitus                  |                |                |                |
| subjects affected / exposed        | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0              |
| Glucose tolerance impaired         |                |                |                |
| subjects affected / exposed        | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0              |
| Hypercholesterolaemia              |                |                |                |
| subjects affected / exposed        | 1 / 48 (2.08%) | 1 / 49 (2.04%) | 1 / 49 (2.04%) |
| occurrences (all)                  | 1              | 1              | 2              |
| Hyperglycaemia                     |                |                |                |
| subjects affected / exposed        | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all)                  | 0              | 0              | 1              |
| Hyperuricaemia                     |                |                |                |
| subjects affected / exposed        | 0 / 48 (0.00%) | 0 / 49 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0              |

| <b>Non-serious adverse events</b>                     | CAM-3001 100 MG  | PLACEBO          |  |
|---|------------------|------------------|--|
| Total subjects affected by non-serious adverse events |                  |                  |  |
| subjects affected / exposed                           | 28 / 48 (58.33%) | 46 / 96 (47.92%) |  |
| Vascular disorders                                    |                  |                  |  |
| Hypertension  |                  |                  |  |
| subjects affected / exposed                           | 0 / 48 (0.00%)   | 2 / 96 (2.08%)   |  |
| occurrences (all)                                     | 0                | 2                |  |
| Venous insufficiency                                  |                  |                  |  |
| subjects affected / exposed                           | 0 / 48 (0.00%)   | 0 / 96 (0.00%)   |  |
| occurrences (all)                                     | 0                | 0                |  |
| General disorders and administration site conditions  |                  |                  |  |
| Asthenia  |                  |                  |  |
| subjects affected / exposed                           | 0 / 48 (0.00%)   | 0 / 96 (0.00%)   |  |
| occurrences (all)                                     | 0                | 0                |  |
| Fatigue   |                  |                  |  |
| subjects affected / exposed                           | 0 / 48 (0.00%)   | 0 / 96 (0.00%)   |  |
| occurrences (all)                                     | 0                | 0                |  |
| Injection site pain                                   |                  |                  |  |
| subjects affected / exposed                           | 1 / 48 (2.08%)   | 0 / 96 (0.00%)   |  |
| occurrences (all)                                     | 2                | 0                |  |

|  |                     |                     |  |
|--|---------------------|---------------------|--|
| Injection site papule<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 48 (0.00%)<br>0 | 0 / 96 (0.00%)<br>0 |  |
| Malaise<br>subjects affected / exposed<br>occurrences (all)  | 1 / 48 (2.08%)<br>1 | 0 / 96 (0.00%)<br>0 |  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)  | 0 / 48 (0.00%)<br>0 | 1 / 96 (1.04%)<br>1 |  |
| Immune system disorders<br>Hypersensitivity<br>subjects affected / exposed<br>occurrences (all)              | 0 / 48 (0.00%)<br>0 | 0 / 96 (0.00%)<br>0 |  |
| Social circumstances<br>Family stress<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 48 (0.00%)<br>0 | 1 / 96 (1.04%)<br>2 |  |
| Reproductive system and breast disorders<br>Amenorrhoea<br>subjects affected / exposed<br>occurrences (all)  | 1 / 48 (2.08%)<br>1 | 0 / 96 (0.00%)<br>0 |  |
| Breast cyst<br>subjects affected / exposed<br>occurrences (all)  | 0 / 48 (0.00%)<br>0 | 1 / 96 (1.04%)<br>1 |  |
| Menopausal symptoms<br>subjects affected / exposed<br>occurrences (all)                                      | 1 / 48 (2.08%)<br>1 | 0 / 96 (0.00%)<br>0 |  |
| Metrorrhagia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 48 (0.00%)<br>0 | 0 / 96 (0.00%)<br>0 |  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all) | 0 / 48 (0.00%)<br>0 | 3 / 96 (3.13%)<br>3 |  |
| Dyspnoea   |                     |                     |  |

|                                      |                |                |  |
|--------------------------------------|----------------|----------------|--|
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)                    | 0              | 0              |  |
| Epistaxis                            |                |                |  |
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)                    | 0              | 0              |  |
| Nasal inflammation                   |                |                |  |
| subjects affected / exposed          | 1 / 48 (2.08%) | 0 / 96 (0.00%) |  |
| occurrences (all)                    | 1              | 0              |  |
| Oropharyngeal pain                   |                |                |  |
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)                    | 0              | 0              |  |
| Upper respiratory tract inflammation |                |                |  |
| subjects affected / exposed          | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)                    | 0              | 2              |  |
| Psychiatric disorders                |                |                |  |
| Acute stress disorder                |                |                |  |
| subjects affected / exposed          | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)                    | 0              | 1              |  |
| Depression                           |                |                |  |
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)                    | 0              | 0              |  |
| Sleep disorder                       |                |                |  |
| subjects affected / exposed          | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)                    | 0              | 1              |  |
| Investigations                       |                |                |  |
| Alanine aminotransferase increased   |                |                |  |
| subjects affected / exposed          | 1 / 48 (2.08%) | 0 / 96 (0.00%) |  |
| occurrences (all)                    | 1              | 0              |  |
| Aspartate aminotransferase increased |                |                |  |
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)                    | 0              | 0              |  |
| Blood cholesterol increased          |                |                |  |
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)                    | 0              | 0              |  |
| Blood triglycerides increased        |                |                |  |

|  |                 |                |  |
|--|-----------------|----------------|--|
| subjects affected / exposed                    | 0 / 48 (0.00%)  | 1 / 96 (1.04%) |  |
| occurrences (all)                              | 0               | 1              |  |
| Blood urine present                            |                 |                |  |
| subjects affected / exposed                    | 0 / 48 (0.00%)  | 1 / 96 (1.04%) |  |
| occurrences (all)                              | 0               | 1              |  |
| Carbon monoxide diffusing capacity decreased   |                 |                |  |
| subjects affected / exposed                    | 5 / 48 (10.42%) | 5 / 96 (5.21%) |  |
| occurrences (all)                              | 6               | 6              |  |
| Eosinophil count increased                     |                 |                |  |
| subjects affected / exposed                    | 0 / 48 (0.00%)  | 0 / 96 (0.00%) |  |
| occurrences (all)                              | 0               | 0              |  |
| Forced expiratory volume decreased             |                 |                |  |
| subjects affected / exposed                    | 0 / 48 (0.00%)  | 0 / 96 (0.00%) |  |
| occurrences (all)                              | 0               | 0              |  |
| Gamma-glutamyltransferase increased            |                 |                |  |
| subjects affected / exposed                    | 0 / 48 (0.00%)  | 1 / 96 (1.04%) |  |
| occurrences (all)                              | 0               | 1              |  |
| Hepatic enzyme increased                       |                 |                |  |
| subjects affected / exposed                    | 1 / 48 (2.08%)  | 2 / 96 (2.08%) |  |
| occurrences (all)                              | 1               | 2              |  |
| Nitrite urine                                  |                 |                |  |
| subjects affected / exposed                    | 0 / 48 (0.00%)  | 0 / 96 (0.00%) |  |
| occurrences (all)                              | 0               | 0              |  |
| Spirometry abnormal                            |                 |                |  |
| subjects affected / exposed                    | 0 / 48 (0.00%)  | 1 / 96 (1.04%) |  |
| occurrences (all)                              | 0               | 1              |  |
| Transaminases increased                        |                 |                |  |
| subjects affected / exposed                    | 1 / 48 (2.08%)  | 0 / 96 (0.00%) |  |
| occurrences (all)                              | 1               | 0              |  |
| Urine albumin/creatinine ratio increased       |                 |                |  |
| subjects affected / exposed                    | 0 / 48 (0.00%)  | 1 / 96 (1.04%) |  |
| occurrences (all)                              | 0               | 1              |  |
| Injury, poisoning and procedural complications |                 |                |  |

|                                     |                |                |  |
|-------------------------------------|----------------|----------------|--|
| Ankle fracture                      |                |                |  |
| subjects affected / exposed         | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)                   | 0              | 0              |  |
| Arthropod bite                      |                |                |  |
| subjects affected / exposed         | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)                   | 0              | 1              |  |
| Contusion                           |                |                |  |
| subjects affected / exposed         | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)                   | 0              | 1              |  |
| Excoriation                         |                |                |  |
| subjects affected / exposed         | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)                   | 0              | 1              |  |
| Foot fracture                       |                |                |  |
| subjects affected / exposed         | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)                   | 0              | 0              |  |
| Joint injury                        |                |                |  |
| subjects affected / exposed         | 1 / 48 (2.08%) | 0 / 96 (0.00%) |  |
| occurrences (all)                   | 1              | 0              |  |
| Toxicity to various agents          |                |                |  |
| subjects affected / exposed         | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)                   | 0              | 1              |  |
| Cardiac disorders                   |                |                |  |
| Aortic valve incompetence           |                |                |  |
| subjects affected / exposed         | 1 / 48 (2.08%) | 0 / 96 (0.00%) |  |
| occurrences (all)                   | 1              | 0              |  |
| Arteriosclerosis coronary artery    |                |                |  |
| subjects affected / exposed         | 1 / 48 (2.08%) | 0 / 96 (0.00%) |  |
| occurrences (all)                   | 1              | 0              |  |
| Cardiac hypertrophy                 |                |                |  |
| subjects affected / exposed         | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)                   | 0              | 1              |  |
| Ventricular extrasystoles           |                |                |  |
| subjects affected / exposed         | 1 / 48 (2.08%) | 0 / 96 (0.00%) |  |
| occurrences (all)                   | 1              | 0              |  |
| Atrioventricular block first degree |                |                |  |



|                                      |                |                |  |
|--------------------------------------|----------------|----------------|--|
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)                    | 0              | 0              |  |
| Palpitations                         |                |                |  |
| subjects affected / exposed          | 1 / 48 (2.08%) | 0 / 96 (0.00%) |  |
| occurrences (all)                    | 1              | 0              |  |
| Supraventricular extrasystoles       |                |                |  |
| subjects affected / exposed          | 1 / 48 (2.08%) | 0 / 96 (0.00%) |  |
| occurrences (all)                    | 1              | 0              |  |
| Nervous system disorders             |                |                |  |
| Autonomic nervous system imbalance   |                |                |  |
| subjects affected / exposed          | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)                    | 0              | 0              |  |
| Head discomfort                      |                |                |  |
| subjects affected / exposed          | 1 / 48 (2.08%) | 0 / 96 (0.00%) |  |
| occurrences (all)                    | 1              | 0              |  |
| Headache                             |                |                |  |
| subjects affected / exposed          | 1 / 48 (2.08%) | 1 / 96 (1.04%) |  |
| occurrences (all)                    | 1              | 1              |  |
| Hypoaesthesia                        |                |                |  |
| subjects affected / exposed          | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)                    | 0              | 1              |  |
| Blood and lymphatic system disorders |                |                |  |
| Anaemia                              |                |                |  |
| subjects affected / exposed          | 1 / 48 (2.08%) | 5 / 96 (5.21%) |  |
| occurrences (all)                    | 1              | 5              |  |
| Eosinophilia                         |                |                |  |
| subjects affected / exposed          | 1 / 48 (2.08%) | 0 / 96 (0.00%) |  |
| occurrences (all)                    | 1              | 0              |  |
| Leukopenia                           |                |                |  |
| subjects affected / exposed          | 0 / 48 (0.00%) | 2 / 96 (2.08%) |  |
| occurrences (all)                    | 0              | 4              |  |
| Lymphopenia                          |                |                |  |
| subjects affected / exposed          | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)                    | 0              | 1              |  |
| Monocytopenia                        |                |                |  |

|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 1 / 48 (2.08%) | 2 / 96 (2.08%) |  |
| occurrences (all)           | 1              | 2              |  |
| Monocytosis                 |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)           | 0              | 1              |  |
| Neutropenia                 |                |                |  |
| subjects affected / exposed | 1 / 48 (2.08%) | 1 / 96 (1.04%) |  |
| occurrences (all)           | 1              | 3              |  |
| Thrombocytopenia            |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Thrombocytosis              |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)           | 0              | 1              |  |
| Ear and labyrinth disorders |                |                |  |
| Ear discomfort              |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)           | 0              | 1              |  |
| Vertigo                     |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)           | 0              | 1              |  |
| Eye disorders               |                |                |  |
| Dry eye                     |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Scleritis                   |                |                |  |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 96 (0.00%) |  |
| occurrences (all)           | 1              | 0              |  |
| Gastrointestinal disorders  |                |                |  |
| Diarrhoea                   |                |                |  |
| subjects affected / exposed | 2 / 48 (4.17%) | 1 / 96 (1.04%) |  |
| occurrences (all)           | 2              | 1              |  |
| Dry mouth                   |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Flatulence                  |                |                |  |

|  |                |                |  |
|--|----------------|----------------|--|
| subjects affected / exposed            | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Gastritis                              |                |                |  |
| subjects affected / exposed            | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Nausea                                 |                |                |  |
| subjects affected / exposed            | 1 / 48 (2.08%) | 0 / 96 (0.00%) |  |
| occurrences (all)                      | 1              | 0              |  |
| Abdominal pain upper                   |                |                |  |
| subjects affected / exposed            | 1 / 48 (2.08%) | 1 / 96 (1.04%) |  |
| occurrences (all)                      | 3              | 1              |  |
| Enterocolitis                          |                |                |  |
| subjects affected / exposed            | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)                      | 0              | 1              |  |
| Gastrooesophageal reflux disease       |                |                |  |
| subjects affected / exposed            | 1 / 48 (2.08%) | 0 / 96 (0.00%) |  |
| occurrences (all)                      | 1              | 0              |  |
| Tooth malformation                     |                |                |  |
| subjects affected / exposed            | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Toothache                              |                |                |  |
| subjects affected / exposed            | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Vomiting                               |                |                |  |
| subjects affected / exposed            | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)                      | 0              | 1              |  |
| Hepatobiliary disorders                |                |                |  |
| Hepatic function abnormal              |                |                |  |
| subjects affected / exposed            | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Skin and subcutaneous tissue disorders |                |                |  |
| Alopecia                               |                |                |  |
| subjects affected / exposed            | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Dermatitis                             |                |                |  |

|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)           | 0              | 3              |  |
| Eczema                      |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)           | 0              | 1              |  |
| Eczema asteatotic           |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Haemorrhage subcutaneous    |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Papule                      |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Pruritus                    |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Rash                        |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 2 / 96 (2.08%) |  |
| occurrences (all)           | 0              | 2              |  |
| Rash maculo-papular         |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Skin exfoliation            |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Spider naevus               |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Urticaria                   |                |                |  |
| subjects affected / exposed | 2 / 48 (4.17%) | 0 / 96 (0.00%) |  |
| occurrences (all)           | 2              | 0              |  |
| Urticaria papular           |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)           | 0              | 1              |  |
| Renal and urinary disorders |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| Haematuria                                      |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)                               | 0              | 1              |  |
| Ketonuria                                       |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)                               | 0              | 0              |  |
| Proteinuria                                     |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)                               | 0              | 0              |  |
| Musculoskeletal and connective tissue disorders |                |                |  |
| Lumbar spinal stenosis                          |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)                               | 0              | 0              |  |
| Bursitis  |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)                               | 0              | 1              |  |
| Muscle spasms                                   |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)                               | 0              | 1              |  |
| Musculoskeletal pain                            |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)                               | 0              | 0              |  |
| Myalgia   |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)                               | 0              | 0              |  |
| Neck pain                                       |                |                |  |
| subjects affected / exposed                     | 1 / 48 (2.08%) | 0 / 96 (0.00%) |  |
| occurrences (all)                               | 1              | 0              |  |
| Osteoarthritis                                  |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)                               | 0              | 0              |  |
| Osteoporosis                                    |                |                |  |
| subjects affected / exposed                     | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)                               | 0              | 1              |  |
| Rheumatoid arthritis                            |                |                |  |

|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)           | 0              | 2              |  |
| Rotator cuff syndrome       |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Spinal osteoarthritis       |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)           | 0              | 1              |  |
| Infections and infestations |                |                |  |
| Acute tonsillitis           |                |                |  |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 96 (0.00%) |  |
| occurrences (all)           | 1              | 0              |  |
| Adenoiditis                 |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)           | 0              | 1              |  |
| Bronchitis                  |                |                |  |
| subjects affected / exposed | 2 / 48 (4.17%) | 1 / 96 (1.04%) |  |
| occurrences (all)           | 2              | 1              |  |
| Bronchitis viral            |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)           | 0              | 1              |  |
| Cellulitis                  |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)           | 0              | 1              |  |
| Cystitis                    |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)           | 0              | 1              |  |
| Enteritis infectious        |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)           | 0              | 1              |  |
| Erysipelas                  |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Gastrointestinal infection  |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |

|   |                      |                     |
|---|----------------------|---------------------|
| Gastrointestinal viral infection<br>subjects affected / exposed<br>occurrences (all)  | 0 / 48 (0.00%)<br>0  | 1 / 96 (1.04%)<br>1 |
| Genitourinary tract infection<br>subjects affected / exposed<br>occurrences (all)     | 0 / 48 (0.00%)<br>0  | 1 / 96 (1.04%)<br>1 |
| Herpangina<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 48 (0.00%)<br>0  | 1 / 96 (1.04%)<br>1 |
| Herpes zoster<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 48 (2.08%)<br>1  | 1 / 96 (1.04%)<br>1 |
| Infected bites<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 48 (0.00%)<br>0  | 1 / 96 (1.04%)<br>1 |
| Influenza<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 48 (0.00%)<br>0  | 1 / 96 (1.04%)<br>1 |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                   | 5 / 48 (10.42%)<br>5 | 5 / 96 (5.21%)<br>5 |
| Oral herpes<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 48 (0.00%)<br>0  | 0 / 96 (0.00%)<br>0 |
| Pharyngitis<br>subjects affected / exposed<br>occurrences (all)                       | 1 / 48 (2.08%)<br>1  | 1 / 96 (1.04%)<br>1 |
| Pyelonephritis<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 48 (0.00%)<br>0  | 0 / 96 (0.00%)<br>0 |
| Respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)       | 0 / 48 (0.00%)<br>0  | 1 / 96 (1.04%)<br>1 |
| Respiratory tract infection viral<br>subjects affected / exposed<br>occurrences (all) | 0 / 48 (0.00%)<br>0  | 0 / 96 (0.00%)<br>0 |

|                                    |                |                |  |
|------------------------------------|----------------|----------------|--|
| Rhinitis                           |                |                |  |
| subjects affected / exposed        | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)                  | 0              | 0              |  |
| Sinusitis                          |                |                |  |
| subjects affected / exposed        | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)                  | 0              | 1              |  |
| Streptococcal infection            |                |                |  |
| subjects affected / exposed        | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)                  | 0              | 1              |  |
| Tinea pedis                        |                |                |  |
| subjects affected / exposed        | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)                  | 0              | 1              |  |
| Tinea versicolour                  |                |                |  |
| subjects affected / exposed        | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)                  | 0              | 0              |  |
| Tonsillitis                        |                |                |  |
| subjects affected / exposed        | 0 / 48 (0.00%) | 0 / 96 (0.00%) |  |
| occurrences (all)                  | 0              | 0              |  |
| Upper respiratory tract infection  |                |                |  |
| subjects affected / exposed        | 2 / 48 (4.17%) | 4 / 96 (4.17%) |  |
| occurrences (all)                  | 2              | 5              |  |
| Urinary tract infection            |                |                |  |
| subjects affected / exposed        | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)                  | 0              | 1              |  |
| Viral infection                    |                |                |  |
| subjects affected / exposed        | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)                  | 0              | 1              |  |
| Metabolism and nutrition disorders |                |                |  |
| Diabetes mellitus                  |                |                |  |
| subjects affected / exposed        | 1 / 48 (2.08%) | 0 / 96 (0.00%) |  |
| occurrences (all)                  | 1              | 0              |  |
| Glucose tolerance impaired         |                |                |  |
| subjects affected / exposed        | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)                  | 0              | 1              |  |
| Hypercholesterolaemia              |                |                |  |



|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)           | 0              | 1              |  |
| Hyperglycaemia              |                |                |  |
| subjects affected / exposed | 0 / 48 (0.00%) | 1 / 96 (1.04%) |  |
| occurrences (all)           | 0              | 1              |  |
| Hyperuricaemia              |                |                |  |
| subjects affected / exposed | 1 / 48 (2.08%) | 0 / 96 (0.00%) |  |
| occurrences (all)           | 1              | 0              |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment  |
|-----------------|--|
| 29 March 2010   | The number of sites and participants were increased and dose escalation process in Japan was described.-Inclusion criterion modified.-A description of unblinding process for analysis of primary endpoint was added to protocol.-Pulmonary functional test (PFTs) and DLCO were allowed to be tested day before dosing.-If screening PFTs were performed within 14 days of dosing on Day 1, then a repeat of PFT was not required.-A description of a potential analysis of primary endpoint was added.-Abnormal laboratory test data were to be reported as an adverse event (AE),the assessment of relationship of AEs as related or not related and the description of overdose and pregnancy were modified.-The language describing the DAS28 requirements was clarified to state that participants were required to have at least moderately active disease as defined by DAS28 $\geq 3.2$ at screening and Day 1 to be included in study. |
| 11 October 2010 | Study blind was amended.   |
| 04 April 2011   | Study blind was amended. – Sponsor was allowed to discontinue dosing. - Study Stopping criteria was modified as: any other safety finding assessed as related to investigational product that, in the opinion of the sponsor, contraindicates further dosing of study participants, was added to the study-stopping criteria. - Sections describing hepatic function abnormality and the recoding and reporting of such events were added to the protocol.   |

Notes:

---

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

---

### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/23234647>