



## Clinical trial results:

### A Phase 2b Study to Evaluate the Efficacy and Safety of Mavrilimumab in Subjects with Moderate-to-Severe Rheumatoid Arthritis

#### Summary

|                          |                      |
|--------------------------|----------------------|
| EudraCT number           | 2011-005634-19       |
| Trial protocol           | HU EE CZ ES DE BG PL |
| Global end of trial date | 29 January 2014      |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 10 February 2016 |
| First version publication date | 10 February 2016 |

#### Trial information

##### Trial identification

|                       |                     |
|-----------------------|---------------------|
| Sponsor protocol code | CD-IA-CAM-3001-1071 |
|-----------------------|---------------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01706926 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |                                                                                         |
|------------------------------|-----------------------------------------------------------------------------------------|
| Sponsor organisation name    | MedImmune, LLC                                                                          |
| Sponsor organisation address | Milstein Building, Granta Park, Cambridge, United Kingdom, CB21 6GH                     |
| Public contact               | Marius Albulescu, Associate Medical Director, MedImmune, LLC, albullescum@medimmune.com |
| Scientific contact           | Marius Albulescu, Associate Medical Director, MedImmune, LLC, albullescum@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                       | 29 January 2014 |
| Is this the analysis of the primary completion data? | No              |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 29 January 2014 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the efficacy of 3 subcutaneous (SC) doses of mavrilimumab compared with placebo in combination with methotrexate (MTX) in participants with moderate-to-severe adult onset 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                          | 27 August 2012 |
| Long term follow-up planned                               | Yes            |
| Long term follow-up rationale                             | Safety         |
| Long term follow-up duration                              | 3 Months       |
| Independent data monitoring committee (IDMC) involvement? | Yes            |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Argentina: 31          |
| Country: Number of subjects enrolled | Bulgaria: 9            |
| Country: Number of subjects enrolled | Chile: 37              |
| Country: Number of subjects enrolled | Colombia: 17           |
| Country: Number of subjects enrolled | Czech Republic: 53     |
| Country: Number of subjects enrolled | Estonia: 23            |
| Country: Number of subjects enrolled | Germany: 9             |
| Country: Number of subjects enrolled | Hungary: 7             |
| Country: Number of subjects enrolled | Poland: 37             |
| Country: Number of subjects enrolled | Russian Federation: 33 |
| Country: Number of subjects enrolled | Serbia: 24             |
| Country: Number of subjects enrolled | South Africa: 2        |
| Country: Number of subjects enrolled | Spain: 1               |
| Country: Number of subjects enrolled | Ukraine: 43            |

|                                    |     |
|------------------------------------|-----|
| Worldwide total number of subjects | 326 |
| EEA total number of subjects       | 139 |

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)                      | 288 |
| From 65 to 84 years                       | 38  |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 420 participants were screened out of which 326 participants were randomized and received investigational product in the study.

### Period 1

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

### Arms

|                              |         |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes     |
| <b>Arm title</b>             | Placebo |

Arm description:

Placebo matched to mavrilimumab (CAM-3001) injection subcutaneously every 2 weeks for 24 weeks in combination with stable dose of methotrexate (7.5 to 25 milligram [mg] per week) through oral or parenteral route.

|                                        |                                 |
|----------------------------------------|---------------------------------|
| Arm type                               | Placebo                         |
| Investigational medicinal product name | Placebo matched to mavrilimumab |
| Investigational medicinal product code |                                 |
| Other name                             |                                 |
| Pharmaceutical forms                   | Solution for injection          |
| Routes of administration               | Subcutaneous use                |

Dosage and administration details:

Placebo matched to mavrilimumab (CAM-3001) injection subcutaneously every 2 weeks for 24 weeks in combination with stable dose of methotrexate (7.5 to 25 milligram [mg] per week) through oral or parenteral route.

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

Arm description:

Mavrilimumab (CAM-3001) 30 mg injection subcutaneously every 2 weeks for 24 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) through oral or parenteral route.

|                                        |                        |
|----------------------------------------|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | Mavrilimumab 30 mg     |
| Investigational medicinal product code | CAM-3001               |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Subcutaneous use       |

Dosage and administration details:

Mavrilimumab (CAM-3001) 30 mg injection subcutaneously every 2 weeks for 24 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) through oral or parenteral route.

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

Arm description:

Mavrilimumab (CAM-3001) 100 mg injection subcutaneously every 2 weeks for 24 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) through oral or parenteral route.

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

|                                        |                        |
|----------------------------------------|------------------------|
| Investigational medicinal product name | Mavrilimumab 100 mg    |
| Investigational medicinal product code | CAM-3001               |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Subcutaneous use       |

Dosage and administration details:

Mavrilimumab (CAM-3001) 100 mg injection subcutaneously every 2 weeks for 24 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) through oral or parenteral route.

|                  |                     |
|------------------|---------------------|
| <b>Arm title</b> | Mavrilimumab 150 mg |
|------------------|---------------------|

Arm description:

Mavrilimumab (CAM-3001) 150 mg injection subcutaneously every 2 weeks for 24 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) through oral or parenteral route.

|                                        |                        |
|----------------------------------------|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | Mavrilimumab 150 mg    |
| Investigational medicinal product code | CAM-3001               |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Subcutaneous use       |

Dosage and administration details:

Mavrilimumab (CAM-3001) 150 mg injection subcutaneously every 2 weeks for 24 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) through oral or parenteral route.

| <b>Number of subjects in period 1</b> | Placebo | Mavrilimumab 30 mg | Mavrilimumab 100 mg |
|---------------------------------------|---------|--------------------|---------------------|
| Started                               | 81      | 81                 | 85                  |
| Completed                             | 75      | 77                 | 79                  |
| Not completed                         | 6       | 4                  | 6                   |
| Consent withdrawn by subject          | 2       | -                  | 1                   |
| Unspecified                           | 4       | 4                  | 4                   |
| Lost to follow-up                     | -       | -                  | 1                   |

| <b>Number of subjects in period 1</b> | Mavrilimumab 150 mg |
|---------------------------------------|---------------------|
| Started                               | 79                  |
| Completed                             | 74                  |
| Not completed                         | 5                   |
| Consent withdrawn by subject          | 2                   |
| Unspecified                           | 3                   |
| Lost to follow-up                     | -                   |

## Baseline characteristics

### Reporting groups

|                                                                                                                                                                                                                                                      |                     |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|
| Reporting group title                                                                                                                                                                                                                                | Placebo             |
| Reporting group description:<br>Placebo matched to mavrilimumab (CAM-3001) injection subcutaneously every 2 weeks for 24 weeks in combination with stable dose of methotrexate (7.5 to 25 milligram [mg] per week) through oral or parenteral route. |                     |
| Reporting group title                                                                                                                                                                                                                                | Mavrilimumab 30 mg  |
| Reporting group description:<br>Mavrilimumab (CAM-3001) 30 mg injection subcutaneously every 2 weeks for 24 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) through oral or parenteral route.                          |                     |
| Reporting group title                                                                                                                                                                                                                                | Mavrilimumab 100 mg |
| Reporting group description:<br>Mavrilimumab (CAM-3001) 100 mg injection subcutaneously every 2 weeks for 24 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) through oral or parenteral route.                         |                     |
| Reporting group title                                                                                                                                                                                                                                | Mavrilimumab 150 mg |
| Reporting group description:<br>Mavrilimumab (CAM-3001) 150 mg injection subcutaneously every 2 weeks for 24 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) through oral or parenteral route.                         |                     |

| Reporting group values | Placebo | Mavrilimumab 30 mg | Mavrilimumab 100 mg |
|------------------------|---------|--------------------|---------------------|
| Number of subjects     | 81      | 81                 | 85                  |
| Age categorical        |         |                    |                     |
| Units: Subjects        |         |                    |                     |

|                     |        |        |        |
|---------------------|--------|--------|--------|
| Age Continuous      |        |        |        |
| Units: years        |        |        |        |
| arithmetic mean     | 52.8   | 51.2   | 50.8   |
| standard deviation  | ± 10.6 | ± 11.6 | ± 11.9 |
| Gender, Male/Female |        |        |        |
| Units: participants |        |        |        |
| Female              | 75     | 70     | 70     |
| Male                | 6      | 11     | 15     |

| Reporting group values | Mavrilimumab 150 mg | Total |  |
|------------------------|---------------------|-------|--|
| Number of subjects     | 79                  | 326   |  |
| Age categorical        |                     |       |  |
| Units: Subjects        |                     |       |  |

|                     |        |     |  |
|---------------------|--------|-----|--|
| Age Continuous      |        |     |  |
| Units: years        |        |     |  |
| arithmetic mean     | 52.6   |     |  |
| standard deviation  | ± 10.3 | -   |  |
| Gender, Male/Female |        |     |  |
| Units: participants |        |     |  |
| Female              | 67     | 282 |  |
| Male                | 12     | 44  |  |



## End points

### End points reporting groups

|                                                                                                                                                                                                                                                      |                     |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|
| Reporting group title                                                                                                                                                                                                                                | Placebo             |
| Reporting group description:<br>Placebo matched to mavrilimumab (CAM-3001) injection subcutaneously every 2 weeks for 24 weeks in combination with stable dose of methotrexate (7.5 to 25 milligram [mg] per week) through oral or parenteral route. |                     |
| Reporting group title                                                                                                                                                                                                                                | Mavrilimumab 30 mg  |
| Reporting group description:<br>Mavrilimumab (CAM-3001) 30 mg injection subcutaneously every 2 weeks for 24 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) through oral or parenteral route.                          |                     |
| Reporting group title                                                                                                                                                                                                                                | Mavrilimumab 100 mg |
| Reporting group description:<br>Mavrilimumab (CAM-3001) 100 mg injection subcutaneously every 2 weeks for 24 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) through oral or parenteral route.                         |                     |
| Reporting group title                                                                                                                                                                                                                                | Mavrilimumab 150 mg |
| Reporting group description:<br>Mavrilimumab (CAM-3001) 150 mg injection subcutaneously every 2 weeks for 24 weeks in combination with stable dose of methotrexate (7.5 to 25 mg per week) through oral or parenteral route.                         |                     |

### Primary: Change From Baseline in Disease Activity Score of 28 Joints Using C-Reactive Protein (DAS28 [CRP]) Score at Day 85

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                    |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Change From Baseline in Disease Activity Score of 28 Joints Using C-Reactive Protein (DAS28 [CRP]) Score at Day 85 |
| End point description:<br>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 modified intent-to-treat (mITT) population analysis set included all participants in the treatment group corresponding to their randomized treatment group. Here "n" signifies participants who were evaluable for this measure for the specified time point for each arm, respectively. |                                                                                                                    |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Primary                                                                                                            |
| End point timeframe:<br>Baseline and Day 85                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                    |

| End point values                    | Placebo         | Mavrilimumab 30 mg | Mavrilimumab 100 mg | Mavrilimumab 150 mg |
|-------------------------------------|-----------------|--------------------|---------------------|---------------------|
| Subject group type                  | Reporting group | Reporting group    | Reporting group     | Reporting group     |
| Number of subjects analysed         | 81              | 81                 | 85                  | 79                  |
| Units: units on a scale             |                 |                    |                     |                     |
| arithmetic mean (standard error)    |                 |                    |                     |                     |
| Baseline (n=81, 81, 85, 79)         | 5.78 (± 0.09)   | 5.73 (± 0.104)     | 5.91 (± 0.096)      | 5.67 (± 0.086)      |
| Change at Day 85 (n=77, 76, 79, 78) | -0.68 (± 0.136) | -1.37 (± 0.136)    | -1.64 (± 0.132)     | -1.9 (± 0.136)      |



## Statistical analyses

| Statistical analysis title                                                                                                                                                                                                                                                                                                                                   | Statistical analysis 1       |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|
| Statistical analysis description:                                                                                                                                                                                                                                                                                                                            |                              |
| Analysis reported for change from baseline in DAS28 (CRP) at Day 85. An estimate of the treatment difference and its 95 percent (%) confidence interval (CI) was computed by means of repeated measures model, adjusted for baseline and including terms for treatment group, visit and treatment by visit interaction. Differences <0 favored mavrilimumab. |                              |
| Comparison groups                                                                                                                                                                                                                                                                                                                                            | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis                                                                                                                                                                                                                                                                                                                      | 162                          |
| Analysis specification                                                                                                                                                                                                                                                                                                                                       | Pre-specified                |
| Analysis type                                                                                                                                                                                                                                                                                                                                                | other                        |
| P-value                                                                                                                                                                                                                                                                                                                                                      | < 0.001                      |
| Method                                                                                                                                                                                                                                                                                                                                                       | Repeated measures model      |
| Parameter estimate                                                                                                                                                                                                                                                                                                                                           | Adjusted mean difference     |
| Point estimate                                                                                                                                                                                                                                                                                                                                               | -0.69                        |
| Confidence interval                                                                                                                                                                                                                                                                                                                                          |                              |
| level                                                                                                                                                                                                                                                                                                                                                        | 95 %                         |
| sides                                                                                                                                                                                                                                                                                                                                                        | 2-sided                      |
| lower limit                                                                                                                                                                                                                                                                                                                                                  | -1.06                        |
| upper limit                                                                                                                                                                                                                                                                                                                                                  | -0.31                        |
| Variability estimate                                                                                                                                                                                                                                                                                                                                         | Standard error of the mean   |
| Dispersion value                                                                                                                                                                                                                                                                                                                                             | 0.193                        |

| Statistical analysis title                                                                                                                                                                                                                                                                                                  | Statistical analysis 2        |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|
| Statistical analysis description:                                                                                                                                                                                                                                                                                           |                               |
| Analysis reported for change from baseline in DAS28 (CRP) at Day 85. An estimate of the treatment difference and its 95% CI was computed by means of repeated measures model, adjusted for baseline and including terms for treatment group, visit and treatment by visit interaction. Differences <0 favored mavrilimumab. |                               |
| Comparison groups                                                                                                                                                                                                                                                                                                           | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis                                                                                                                                                                                                                                                                                     | 166                           |
| Analysis specification                                                                                                                                                                                                                                                                                                      | Pre-specified                 |
| Analysis type                                                                                                                                                                                                                                                                                                               | other                         |
| P-value                                                                                                                                                                                                                                                                                                                     | < 0.001                       |
| Method                                                                                                                                                                                                                                                                                                                      | Repeated measures model       |
| Parameter estimate                                                                                                                                                                                                                                                                                                          | Adjusted mean difference      |
| Point estimate                                                                                                                                                                                                                                                                                                              | -0.96                         |
| Confidence interval                                                                                                                                                                                                                                                                                                         |                               |
| level                                                                                                                                                                                                                                                                                                                       | 95 %                          |
| sides                                                                                                                                                                                                                                                                                                                       | 2-sided                       |
| lower limit                                                                                                                                                                                                                                                                                                                 | -1.33                         |
| upper limit                                                                                                                                                                                                                                                                                                                 | -0.58                         |

|                      |                            |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value     | 0.19                       |

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

Statistical analysis description:

Analysis reported for change from baseline in DAS28 (CRP) at Day 85. An estimate of the treatment difference and its 95% CI was computed by means of repeated measures model, adjusted for baseline and including terms for treatment group, visit and treatment by visit interaction. Differences <0 favored mavrilimumab.

|                                         |                               |
|-----------------------------------------|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 150 mg |
| Number of subjects included in analysis | 160                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 0.001                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted mean difference      |
| Point estimate                          | -1.22                         |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -1.6                          |
| upper limit                             | -0.84                         |
| Variability estimate                    | Standard error of the mean    |
| Dispersion value                        | 0.193                         |

### **Primary: Percentage of Participants who Achieved American College of Rheumatology 20 (ACR20) Responses at Day 169**

|                 |                                                                                                          |
|-----------------|----------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Participants who Achieved American College of Rheumatology 20 (ACR20) Responses at Day 169 |
|-----------------|----------------------------------------------------------------------------------------------------------|

End point description:

ACR20 was defined as  $\geq 20$  percent (%) improvement, in: SJC and TJC and  $\geq 20\%$  improvement 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 CRP. The mITT population analysis set included all participants in the treatment group corresponding to their randomized treatment group.

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

End point timeframe:

Day 169

| <b>End point values</b>           | Placebo         | Mavrilimumab 30 mg | Mavrilimumab 100 mg | Mavrilimumab 150 mg |
|-----------------------------------|-----------------|--------------------|---------------------|---------------------|
| Subject group type                | Reporting group | Reporting group    | Reporting group     | Reporting group     |
| Number of subjects analysed       | 81              | 81                 | 85                  | 79                  |
| Units: percentage of participants |                 |                    |                     |                     |
| number (not applicable)           | 24.7            | 50.6               | 61.2                | 73.4                |

## Statistical analyses

|                                         |                              |
|-----------------------------------------|------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 1       |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 162                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other                        |
| P-value                                 | < 0.001                      |
| Method                                  | Regression, Logistic         |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 25.9                         |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | 11.5                         |
| upper limit                             | 40.3                         |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 2        |
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 166                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 0.001                       |
| Method                                  | Regression, Logistic          |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | 36.5                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 22.5                          |
| upper limit                             | 50.5                          |

|                                   |                               |
|-----------------------------------|-------------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 3        |
| Comparison groups                 | Placebo v Mavrilimumab 150 mg |

|                                         |                      |
|-----------------------------------------|----------------------|
| Number of subjects included in analysis | 160                  |
| Analysis specification                  | Pre-specified        |
| Analysis type                           | other                |
| P-value                                 | < 0.001              |
| Method                                  | Regression, Logistic |
| Parameter estimate                      | Percent difference   |
| Point estimate                          | 48.7                 |
| Confidence interval                     |                      |
| level                                   | 95 %                 |
| sides                                   | 2-sided              |
| lower limit                             | 35.2                 |
| upper limit                             | 62.3                 |

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

|                 |                                                                                                                                  |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Participants With Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs) |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------|

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 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 | Secondary |
|----------------|-----------|

End point timeframe:

Baseline up to Day 169

| End point values                  | Placebo         | Mavrilimumab 30 mg | Mavrilimumab 100 mg | Mavrilimumab 150 mg |
|-----------------------------------|-----------------|--------------------|---------------------|---------------------|
| Subject group type                | Reporting group | Reporting group    | Reporting group     | Reporting group     |
| Number of subjects analysed       | 81              | 81                 | 85                  | 79                  |
| Units: percentage of participants |                 |                    |                     |                     |
| number (not applicable)           |                 |                    |                     |                     |
| TEAEs                             | 46.9            | 50.6               | 42.4                | 54.4                |
| TESAEs                            | 1.2             | 4.9                | 5.9                 | 2.5                 |

### Statistical analyses

No statistical analyses for this end point

### Secondary: 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 |
|-----------------|-------------------------------------------------------------------------------------------------------------------|

## End point description:

Any medically significant change in laboratory evaluations were recorded as adverse events. Following parameters were analyzed for laboratory examination: hematology (haemoglobin, absolute neutrophil count, leukocyte count, platelet count), serum chemistry (alanine transaminase, aspartate transaminase, bilirubin, gamma-glutamyl transferase), other serum chemistry (low-density lipoprotein cholesterol, triglycerides), and urinalysis. The safety population included all participants who received any dose of investigational product.

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

End point timeframe:

Baseline up to Day 169

| End point values                     | Placebo         | Mavrilimumab<br>30 mg | Mavrilimumab<br>100 mg | Mavrilimumab<br>150 mg |
|--------------------------------------|-----------------|-----------------------|------------------------|------------------------|
| Subject group type                   | Reporting group | Reporting group       | Reporting group        | Reporting group        |
| Number of subjects analysed          | 81              | 81                    | 85                     | 79                     |
| Units: participants                  |                 |                       |                        |                        |
| Anemia                               | 1               | 1                     | 0                      | 0                      |
| Eosinophilia                         | 0               | 0                     | 1                      | 0                      |
| Leukocytosis                         | 2               | 0                     | 0                      | 0                      |
| Lymphopenia                          | 0               | 0                     | 0                      | 1                      |
| Neutropenia                          | 1               | 0                     | 0                      | 3                      |
| Alanine aminotransferase increased   | 0               | 1                     | 1                      | 1                      |
| Aspartate aminotransferase increased | 0               | 1                     | 1                      | 0                      |
| Gamma-glutamyltransferase increased  | 0               | 1                     | 0                      | 0                      |
| Hypertransaminasaemia                | 0               | 0                     | 2                      | 2                      |
| Dislipidaemia                        | 0               | 0                     | 1                      | 0                      |
| Hypercholesterolaemia                | 1               | 0                     | 1                      | 0                      |
| Hyperlipidaemia                      | 0               | 2                     | 0                      | 3                      |
| Hyperkalaemia                        | 0               | 0                     | 0                      | 1                      |

## Statistical analyses

No statistical analyses for this end point

**Secondary: 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) |
|-----------------|--------------------------------------------------------------------------------------------------------|

## End point description:

Vital sign assessments included blood pressure, pulse rate, temperature, weight 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 | Secondary |
|----------------|-----------|

End point timeframe:

Baseline up to Day 169

| End point values            | Placebo         | Mavrilimumab 30 mg | Mavrilimumab 100 mg | Mavrilimumab 150 mg |
|-----------------------------|-----------------|--------------------|---------------------|---------------------|
| Subject group type          | Reporting group | Reporting group    | Reporting group     | Reporting group     |
| Number of subjects analysed | 81              | 81                 | 85                  | 79                  |
| Units: participants         |                 |                    |                     |                     |
| Hypertension                | 2               | 4                  | 4                   | 3                   |
| Weight increased            | 1               | 1                  | 1                   | 0                   |
| Pyrexia                     | 0               | 1                  | 0                   | 0                   |
| Hot flush                   | 0               | 0                  | 1                   | 0                   |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Pulmonary Function Test Values Below Threshold Values at Day 169

|                 |                                                                                |
|-----------------|--------------------------------------------------------------------------------|
| End point title | Percentage of Pulmonary Function Test Values Below Threshold Values at Day 169 |
|-----------------|--------------------------------------------------------------------------------|

End point description:

Pulmonary function testing were performed by spirometry to assess forced expiratory volume in 1 second (FEV1), forced expiratory volume in 6 second (FEV6), and forced vital capacity (FVC). FEV1 was the maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration. FEV6 was the maximal volume of air exhaled in the 6 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 percentage of predicted values of these pulmonary function tests were calculated based on decreases from baseline and categorized as less than or equal to ( $\leq$ ) 15%, more than ( $>$ ) 15 to  $\leq$  20%, and  $>$  20%. The safety population included all participants who received any dose of investigational product. Here "n" signifies participants who were evaluable for this measure for the specified threshold value mentioned parameter for each arm, respectively.

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

End point timeframe:

Day 169

| End point values                        | Placebo         | Mavrilimumab 30 mg | Mavrilimumab 100 mg | Mavrilimumab 150 mg |
|-----------------------------------------|-----------------|--------------------|---------------------|---------------------|
| Subject group type                      | Reporting group | Reporting group    | Reporting group     | Reporting group     |
| Number of subjects analysed             | 81              | 81                 | 85                  | 79                  |
| Units: percent of pulmonary test values |                 |                    |                     |                     |
| number (not applicable)                 |                 |                    |                     |                     |
| FEV1 $\leq$ 15% (n=42,67,75,75)         | 97.6            | 98.5               | 96                  | 89.3                |
| FEV1 $>$ 15 to 20% (n=42,67,75,75)      | 0               | 0                  | 1.3                 | 6.7                 |
| FEV1 $>$ 20% (n=42,67,75,75)            | 2.4             | 1.5                | 2.7                 | 4                   |
| FEV6 $\leq$ 15% (n=41,66,71,68)         | 97.6            | 97                 | 94.4                | 89.7                |
| FEV6 $>$ 15 to 20% (n=41,66,71,68)      | 0               | 1.5                | 1.4                 | 1.5                 |
| FEV6 $>$ 20% (n=41,66,71,68)            | 2.4             | 1.5                | 4.2                 | 8.8                 |
| FVC $\leq$ 15% (n=42,67,75,75)          | 97.6            | 98.5               | 94.7                | 94.7                |

|                                |     |     |     |     |
|--------------------------------|-----|-----|-----|-----|
| FVC >15 to 20% (n=42,67,75,75) | 0   | 0   | 1.3 | 2.7 |
| FVC >20% (n=42,67,75,75)       | 2.4 | 1.5 | 4   | 2.7 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Dyspnea Score at Day 169

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                          |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Dyspnea Score at Day 169 |
| End point description:<br>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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Secondary                |
| End point timeframe:<br>Day 169                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                          |

| End point values                     | Placebo         | Mavrilimumab 30 mg | Mavrilimumab 100 mg | Mavrilimumab 150 mg |
|--------------------------------------|-----------------|--------------------|---------------------|---------------------|
| Subject group type                   | Reporting group | Reporting group    | Reporting group     | Reporting group     |
| Number of subjects analysed          | 41              | 65                 | 73                  | 74                  |
| Units: units on a scale              |                 |                    |                     |                     |
| arithmetic mean (standard deviation) | 0.38 (± 0.62)   | 0.22 (± 0.54)      | 0.32 (± 0.73)       | 0.28 (± 0.64)       |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Oxygen Saturation Level at Day 169

|                                                                                                                                                                                                                                                                                                                                          |                                    |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                          | Oxygen Saturation Level at Day 169 |
| End point description:<br>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                                                                                                                                                                                                                                                                                                                           | Secondary                          |
| End point timeframe:<br>Day 169                                                                                                                                                                                                                                                                                                          |                                    |

| End point values                     | Placebo         | Mavrilimumab 30 mg | Mavrilimumab 100 mg | Mavrilimumab 150 mg |
|--------------------------------------|-----------------|--------------------|---------------------|---------------------|
| Subject group type                   | Reporting group | Reporting group    | Reporting group     | Reporting group     |
| Number of subjects analysed          | 40              | 65                 | 73                  | 74                  |
| Units: percent saturation            |                 |                    |                     |                     |
| arithmetic mean (standard deviation) | 97.4 (± 1.4)    | 97.4 (± 1.1)       | 97.4 (± 1.1)        | 97.3 (± 1.2)        |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants who Achieved American College of Rheumatology 50 (ACR50) Responses at Day 169

|                 |                                                                                                          |
|-----------------|----------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Participants who Achieved American College of Rheumatology 50 (ACR50) Responses at Day 169 |
|-----------------|----------------------------------------------------------------------------------------------------------|

End point description:

ACR50 was defined as  $\geq 50\%$  improvement, in: SJC and TJC and  $\geq 50\%$  improvement 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. The mITT population analysis set included all participants in the treatment group corresponding to their randomized treatment group.

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

End point timeframe:

Day 169

| End point values                  | Placebo         | Mavrilimumab 30 mg | Mavrilimumab 100 mg | Mavrilimumab 150 mg |
|-----------------------------------|-----------------|--------------------|---------------------|---------------------|
| Subject group type                | Reporting group | Reporting group    | Reporting group     | Reporting group     |
| Number of subjects analysed       | 81              | 81                 | 85                  | 79                  |
| Units: percentage of participants |                 |                    |                     |                     |
| number (not applicable)           | 12.3            | 28.4               | 25.9                | 40.5                |

## Statistical analyses

|                                         |                              |
|-----------------------------------------|------------------------------|
| Statistical analysis title              | Statistical analysis 1       |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 162                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other                        |
| P-value                                 | = 0.013                      |
| Method                                  | Regression, Logistic         |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 16                           |



|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 3.9     |
| upper limit         | 28.2    |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 2        |
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 166                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | = 0.03                        |
| Method                                  | Regression, Logistic          |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | 13.5                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 1.8                           |
| upper limit                             | 25.3                          |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 3        |
| Comparison groups                       | Placebo v Mavrilimumab 150 mg |
| Number of subjects included in analysis | 160                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 0.001                       |
| Method                                  | Regression, Logistic          |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | 28.2                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 15.2                          |
| upper limit                             | 41.1                          |

### **Secondary: Percentage of Participants who Achieved American College of Rheumatology 70 (ACR70) Responses at Day 169**

|                 |                                                                                                          |
|-----------------|----------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Participants who Achieved American College of Rheumatology 70 (ACR70) Responses at Day 169 |
|-----------------|----------------------------------------------------------------------------------------------------------|

#### **End point description:**

ACR70 was defined as  $\geq 70\%$  improvement, in: SJC and TJC and  $\geq 70\%$  improvement 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. The mITT population analysis set included all participants in the treatment group

corresponding to their randomized treatment group.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Day 169              |           |

| End point values                  | Placebo         | Mavrilimumab<br>30 mg | Mavrilimumab<br>100 mg | Mavrilimumab<br>150 mg |
|-----------------------------------|-----------------|-----------------------|------------------------|------------------------|
| Subject group type                | Reporting group | Reporting group       | Reporting group        | Reporting group        |
| Number of subjects analysed       | 81              | 81                    | 85                     | 79                     |
| Units: percentage of participants |                 |                       |                        |                        |
| number (not applicable)           | 3.7             | 12.3                  | 10.6                   | 13.9                   |

### Statistical analyses

|                                         |                              |
|-----------------------------------------|------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 1       |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 162                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other                        |
| P-value                                 | = 0.079                      |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 8.6                          |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | 0.4                          |
| upper limit                             | 16.9                         |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 2        |
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 166                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | = 0.133                       |
| Method                                  | Fisher exact                  |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | 6.9                           |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -0.8                          |
| upper limit                             | 14.6                          |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 3        |
| Comparison groups                       | Placebo v Mavrilimumab 150 mg |
| Number of subjects included in analysis | 160                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | = 0.026                       |
| Method                                  | Fisher exact                  |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | 10.2                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 1.5                           |
| upper limit                             | 18.9                          |

## Secondary: American College of Rheumatology (ACRn) Score at Day 169

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                          |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | American College of Rheumatology (ACRn) Score at Day 169 |
| 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 mITT population analysis set included all participants in the treatment group corresponding to their randomized treatment group. |                                                          |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Secondary                                                |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                          |
| Day 169                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                          |

| End point values                 | Placebo         | Mavrilimumab 30 mg | Mavrilimumab 100 mg | Mavrilimumab 150 mg |
|----------------------------------|-----------------|--------------------|---------------------|---------------------|
| Subject group type               | Reporting group | Reporting group    | Reporting group     | Reporting group     |
| Number of subjects analysed      | 81              | 81                 | 85                  | 79                  |
| Units: units on a scale          |                 |                    |                     |                     |
| arithmetic mean (standard error) | 13.25 (± 4.63)  | 29.04 (± 3.828)    | 30.24 (± 3.623)     | 40.72 (± 3.644)     |

## Statistical analyses

|                                   |                              |
|-----------------------------------|------------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 1       |
| Comparison groups                 | Placebo v Mavrilimumab 30 mg |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 162                        |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other                      |
| P-value                                 | = 0.009                    |
| Method                                  | Repeated measures model    |
| Parameter estimate                      | Adjusted Mean difference   |
| Point estimate                          | 15.79                      |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | 3.96                       |
| upper limit                             | 27.61                      |
| Variability estimate                    | Standard error of the mean |
| Dispersion value                        | 6.007                      |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 2        |
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 166                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | = 0.004                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted mean difference      |
| Point estimate                          | 16.99                         |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 5.42                          |
| upper limit                             | 28.56                         |
| Variability estimate                    | Standard error of the mean    |
| Dispersion value                        | 5.879                         |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 3        |
| Comparison groups                       | Placebo v Mavrilimumab 150 mg |
| Number of subjects included in analysis | 160                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 0.001                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted mean difference      |
| Point estimate                          | 27.47                         |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 15.87                         |
| upper limit                             | 39.07                         |

|                      |                            |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value     | 5.892                      |

## Secondary: Percentage of Participants who Achieved DAS28 (CRP) Response by European League Against Rheumatism (EULAR) Category at Day 169

|                 |                                                                                                                                |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Participants who Achieved DAS28 (CRP) Response by European League Against Rheumatism (EULAR) Category at Day 169 |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------|

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  $>1.2$  with baseline DAS28 (CRP)  $<3.2$ ; moderate response: change from baseline  $>1.2$  with baseline DAS28 (CRP)  $\geq 3.2$  to less than or equal to ( $=$ )  $5.1$  or change from baseline  $\geq 0.6$  to  $\leq 1.2$  with baseline DAS28 (CRP)  $\geq 3.2$  to  $\leq 5.1$ ; no response: change from baseline  $<0.6$  or change from baseline  $\geq 0.6$  and  $\leq 1.2$  with baseline DAS28 (CRP)  $>5.1$ . The mITT population analysis set included all participants in the treatment group corresponding to their randomized treatment group.

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

End point timeframe:

Day 169

| End point values                  | Placebo         | Mavrilimumab 30 mg | Mavrilimumab 100 mg | Mavrilimumab 150 mg |
|-----------------------------------|-----------------|--------------------|---------------------|---------------------|
| Subject group type                | Reporting group | Reporting group    | Reporting group     | Reporting group     |
| Number of subjects analysed       | 81              | 81                 | 85                  | 79                  |
| Units: percentage of participants |                 |                    |                     |                     |
| number (not applicable)           |                 |                    |                     |                     |
| No response                       | 65.4            | 30.9               | 28.2                | 19                  |
| Moderate response                 | 25.9            | 35.8               | 40                  | 41.8                |
| Good response                     | 8.6             | 33.3               | 31.8                | 39.2                |

## Statistical analyses

|                                         |                              |
|-----------------------------------------|------------------------------|
| Statistical analysis title              | Statistical analysis 1       |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 162                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other                        |
| P-value                                 | $< 0.001$                    |
| Method                                  | Proportional odds analysis   |
| Parameter estimate                      | Odds ratio (OR)              |
| Point estimate                          | 4.7                          |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | 2.56                         |
| upper limit                             | 8.8                          |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 2        |
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 166                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 0.001                       |
| Method                                  | Proportional odds analysis    |
| Parameter estimate                      | Odds ratio (OR)               |
| Point estimate                          | 4.81                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 2.64                          |
| upper limit                             | 8.92                          |

|                                                                                                                                                                                                                                                                                                                             |                               |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                                                                                           | Statistical analysis 3        |
| Statistical analysis description:                                                                                                                                                                                                                                                                                           |                               |
| Analysis reported for change from baseline in DAS28 (CRP) at Day 85. An estimate of the treatment difference and its 95% CI was computed by means of repeated measures model, adjusted for baseline and including terms for treatment group, visit and treatment by visit interaction. Differences <0 favored mavrilimumab. |                               |
| Comparison groups                                                                                                                                                                                                                                                                                                           | Placebo v Mavrilimumab 150 mg |
| Number of subjects included in analysis                                                                                                                                                                                                                                                                                     | 160                           |
| Analysis specification                                                                                                                                                                                                                                                                                                      | Pre-specified                 |
| Analysis type                                                                                                                                                                                                                                                                                                               | other                         |
| P-value                                                                                                                                                                                                                                                                                                                     | < 0.001                       |
| Method                                                                                                                                                                                                                                                                                                                      | Proportional odds analysis    |
| Parameter estimate                                                                                                                                                                                                                                                                                                          | Odds ratio (OR)               |
| Point estimate                                                                                                                                                                                                                                                                                                              | 7.11                          |
| Confidence interval                                                                                                                                                                                                                                                                                                         |                               |
| level                                                                                                                                                                                                                                                                                                                       | 95 %                          |
| sides                                                                                                                                                                                                                                                                                                                       | 2-sided                       |
| lower limit                                                                                                                                                                                                                                                                                                                 | 3.85                          |
| upper limit                                                                                                                                                                                                                                                                                                                 | 13.4                          |

### **Secondary: Percentage of Participants With DAS28 (CRP) Remission and Low Disease Activity at Day 169**

|                 |                                                                                           |
|-----------------|-------------------------------------------------------------------------------------------|
| End point title | Percentage of Participants With DAS28 (CRP) Remission and Low Disease Activity at Day 169 |
|-----------------|-------------------------------------------------------------------------------------------|

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. Remission was defined as less than 2.6 DAS28 (CRP) score. Low disease activity was defined as less than 3.2 DAS28 (CRP) score. The mITT population analysis set included all participants in the treatment group corresponding

to their randomized treatment group.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Day 169              |           |

| End point values                  | Placebo         | Mavrilimumab<br>30 mg | Mavrilimumab<br>100 mg | Mavrilimumab<br>150 mg |
|-----------------------------------|-----------------|-----------------------|------------------------|------------------------|
| Subject group type                | Reporting group | Reporting group       | Reporting group        | Reporting group        |
| Number of subjects analysed       | 81              | 81                    | 85                     | 79                     |
| Units: percentage of participants |                 |                       |                        |                        |
| number (not applicable)           |                 |                       |                        |                        |
| DAS28 (CRP) Remission             | 4.9             | 21                    | 17.6                   | 19                     |
| Low Disease Activity              | 8.6             | 33.3                  | 31.8                   | 41.8                   |

## Statistical analyses

|                                                                                                                                                                     |                              |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                   | Statistical analysis 1       |
| Statistical analysis description:<br>DAS28 (CRP) remission: p-value estimated from fisher's exact test when number of placebo or active responders was less than 5. |                              |
| Comparison groups                                                                                                                                                   | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis                                                                                                                             | 162                          |
| Analysis specification                                                                                                                                              | Pre-specified                |
| Analysis type                                                                                                                                                       | other                        |
| P-value                                                                                                                                                             | = 0.004                      |
| Method                                                                                                                                                              | Fisher exact                 |
| Parameter estimate                                                                                                                                                  | Percent difference           |
| Point estimate                                                                                                                                                      | 16                           |
| Confidence interval                                                                                                                                                 |                              |
| level                                                                                                                                                               | 95 %                         |
| sides                                                                                                                                                               | 2-sided                      |
| lower limit                                                                                                                                                         | 6                            |
| upper limit                                                                                                                                                         | 26.1                         |

|                                                                                                                                                                     |                               |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                   | Statistical analysis 2        |
| Statistical analysis description:<br>DAS28 (CRP) remission: p-value estimated from fisher's exact test when number of placebo or active responders was less than 5. |                               |
| Comparison groups                                                                                                                                                   | Placebo v Mavrilimumab 100 mg |

|                                         |                    |
|-----------------------------------------|--------------------|
| Number of subjects included in analysis | 166                |
| Analysis specification                  | Pre-specified      |
| Analysis type                           | other              |
| P-value                                 | = 0.014            |
| Method                                  | Fisher exact       |
| Parameter estimate                      | Percent difference |
| Point estimate                          | 12.7               |
| Confidence interval                     |                    |
| level                                   | 95 %               |
| sides                                   | 2-sided            |
| lower limit                             | 3.3                |
| upper limit                             | 22.1               |

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

Statistical analysis description:

DAS28 (CRP) remission: p-value estimated from fisher's exact test when number of placebo or active responders was less than 5.

|                                         |                               |
|-----------------------------------------|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 150 mg |
| Number of subjects included in analysis | 160                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | = 0.007                       |
| Method                                  | Fisher exact                  |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | 14                            |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 4.2                           |
| upper limit                             | 23.9                          |

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

Statistical analysis description:

The analysis reported DAS28 (CRP) low disease activity response.

|                                         |                              |
|-----------------------------------------|------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 162                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other                        |
| P-value                                 | < 0.001                      |
| Method                                  | Regression, Logistic         |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 24.7                         |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | 12.7                         |
| upper limit                             | 36.6                         |



|                                                                                                       |                               |
|-------------------------------------------------------------------------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>                                                                     | Statistical analysis 5        |
| Statistical analysis description:<br>The analysis reported DAS28 (CRP) low disease activity response. |                               |
| Comparison groups                                                                                     | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis                                                               | 166                           |
| Analysis specification                                                                                | Pre-specified                 |
| Analysis type                                                                                         | other                         |
| P-value                                                                                               | < 0.001                       |
| Method                                                                                                | Regression, Logistic          |
| Parameter estimate                                                                                    | Percent difference            |
| Point estimate                                                                                        | 23.1                          |
| Confidence interval                                                                                   |                               |
| level                                                                                                 | 95 %                          |
| sides                                                                                                 | 2-sided                       |
| lower limit                                                                                           | 11.5                          |
| upper limit                                                                                           | 34.8                          |

|                                                                                                       |                               |
|-------------------------------------------------------------------------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>                                                                     | Statistical analysis 6        |
| Statistical analysis description:<br>The analysis reported DAS28 (CRP) low disease activity response. |                               |
| Comparison groups                                                                                     | Placebo v Mavrilimumab 150 mg |
| Number of subjects included in analysis                                                               | 160                           |
| Analysis specification                                                                                | Pre-specified                 |
| Analysis type                                                                                         | other                         |
| P-value                                                                                               | < 0.001                       |
| Method                                                                                                | Regression, Logistic          |
| Parameter estimate                                                                                    | Percent difference            |
| Point estimate                                                                                        | 33.1                          |
| Confidence interval                                                                                   |                               |
| level                                                                                                 | 95 %                          |
| sides                                                                                                 | 2-sided                       |
| lower limit                                                                                           | 20.7                          |
| upper limit                                                                                           | 45.6                          |

## Secondary: Mean Change From Baseline in Swollen and Tender Joint Count at Day 169

|                 |                                                                        |
|-----------------|------------------------------------------------------------------------|
| End point title | Mean Change From Baseline in Swollen and Tender Joint Count at Day 169 |
|-----------------|------------------------------------------------------------------------|

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 mITT population analysis set included all participants in the treatment group corresponding to their randomized treatment group. 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 169 |           |

| End point values                       | Placebo         | Mavrilimumab 30 mg | Mavrilimumab 100 mg | Mavrilimumab 150 mg |
|----------------------------------------|-----------------|--------------------|---------------------|---------------------|
| Subject group type                     | Reporting group | Reporting group    | Reporting group     | Reporting group     |
| Number of subjects analysed            | 81              | 81                 | 85                  | 79                  |
| Units: joint count                     |                 |                    |                     |                     |
| arithmetic mean (standard error)       |                 |                    |                     |                     |
| SJC: Baseline (n=81,81,85,79)          | 14.44 (± 0.765) | 17.8 (± 1.126)     | 16.82 (± 0.93)      | 15.72 (± 0.795)     |
| SJC: Change at Day 169 (n=40,65,73,74) | -4.97 (± 0.932) | -10.65 (± 0.809)   | -11.18 (± 0.771)    | -11.96 (± 0.787)    |
| TJC: Baseline (n=81,81,85,79)          | 26.26 (± 1.25)  | 27.48 (± 1.553)    | 26.96 (± 1.544)     | 26.7 (± 1.284)      |
| TJC: Change at Day 169 (n=40,65,73,74) | -7.9 (± 1.447)  | -15.14 (± 1.265)   | -16.35 (± 1.207)    | -18.32 (± 1.234)    |

## Statistical analyses

|                                                                               |                              |
|-------------------------------------------------------------------------------|------------------------------|
| <b>Statistical analysis title</b>                                             | Statistical analysis 1       |
| Statistical analysis description:                                             |                              |
| Analysis reported for change from baseline in swollen joint count at Day 169. |                              |
| Comparison groups                                                             | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis                                       | 162                          |
| Analysis specification                                                        | Pre-specified                |
| Analysis type                                                                 | other                        |
| P-value                                                                       | < 0.001                      |
| Method                                                                        | Repeated measures model      |
| Parameter estimate                                                            | Adjusted mean difference     |
| Point estimate                                                                | -5.68                        |
| Confidence interval                                                           |                              |
| level                                                                         | 95 %                         |
| sides                                                                         | 2-sided                      |
| lower limit                                                                   | -8.12                        |
| upper limit                                                                   | -3.24                        |
| Variability estimate                                                          | Standard error of the mean   |
| Dispersion value                                                              | 1.237                        |

|                                                                               |                               |
|-------------------------------------------------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>                                             | Statistical analysis 2        |
| Statistical analysis description:                                             |                               |
| Analysis reported for change from baseline in swollen joint count at Day 169. |                               |
| Comparison groups                                                             | Placebo v Mavrilimumab 100 mg |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 166                        |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other                      |
| P-value                                 | < 0.001                    |
| Method                                  | Repeated measures model    |
| Parameter estimate                      | Adjusted mean difference   |
| Point estimate                          | -6.21                      |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | -8.6                       |
| upper limit                             | -3.82                      |
| Variability estimate                    | Standard error of the mean |
| Dispersion value                        | 1.211                      |

|                                                                               |                               |
|-------------------------------------------------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>                                             | Statistical analysis 3        |
| Statistical analysis description:                                             |                               |
| Analysis reported for change from baseline in swollen joint count at Day 169. |                               |
| Comparison groups                                                             | Placebo v Mavrilimumab 150 mg |
| Number of subjects included in analysis                                       | 160                           |
| Analysis specification                                                        | Pre-specified                 |
| Analysis type                                                                 | other                         |
| P-value                                                                       | < 0.001                       |
| Method                                                                        | Repeated measures model       |
| Parameter estimate                                                            | Adjusted mean difference      |
| Point estimate                                                                | -7                            |
| Confidence interval                                                           |                               |
| level                                                                         | 95 %                          |
| sides                                                                         | 2-sided                       |
| lower limit                                                                   | -9.4                          |
| upper limit                                                                   | -4.59                         |
| Variability estimate                                                          | Standard error of the mean    |
| Dispersion value                                                              | 1.219                         |

|                                                                              |                              |
|------------------------------------------------------------------------------|------------------------------|
| <b>Statistical analysis title</b>                                            | Statistical analysis 4       |
| Statistical analysis description:                                            |                              |
| Analysis reported for change from baseline in tender joint count at Day 169. |                              |
| Comparison groups                                                            | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis                                      | 162                          |
| Analysis specification                                                       | Pre-specified                |
| Analysis type                                                                | other                        |
| P-value                                                                      | < 0.001                      |
| Method                                                                       | Repeated measures model      |
| Parameter estimate                                                           | Adjusted mean difference     |
| Point estimate                                                               | -7.24                        |

|                      |                            |
|----------------------|----------------------------|
| Confidence interval  |                            |
| level                | 95 %                       |
| sides                | 2-sided                    |
| lower limit          | -11.02                     |
| upper limit          | -3.45                      |
| Variability estimate | Standard error of the mean |
| Dispersion value     | 1.922                      |

|                                                                              |                               |
|------------------------------------------------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>                                            | Statistical analysis 5        |
| Statistical analysis description:                                            |                               |
| Analysis reported for change from baseline in tender joint count at Day 169. |                               |
| Comparison groups                                                            | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis                                      | 166                           |
| Analysis specification                                                       | Pre-specified                 |
| Analysis type                                                                | other                         |
| P-value                                                                      | < 0.001                       |
| Method                                                                       | Repeated measures model       |
| Parameter estimate                                                           | Adjusted mean difference      |
| Point estimate                                                               | -8.45                         |
| Confidence interval                                                          |                               |
| level                                                                        | 95 %                          |
| sides                                                                        | 2-sided                       |
| lower limit                                                                  | -12.16                        |
| upper limit                                                                  | -4.74                         |
| Variability estimate                                                         | Standard error of the mean    |
| Dispersion value                                                             | 1.884                         |

|                                                                              |                               |
|------------------------------------------------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>                                            | Statistical analysis 6        |
| Statistical analysis description:                                            |                               |
| Analysis reported for change from baseline in tender joint count at Day 169. |                               |
| Comparison groups                                                            | Placebo v Mavrilimumab 150 mg |
| Number of subjects included in analysis                                      | 160                           |
| Analysis specification                                                       | Pre-specified                 |
| Analysis type                                                                | other                         |
| P-value                                                                      | < 0.001                       |
| Method                                                                       | Repeated measures model       |
| Parameter estimate                                                           | Adjusted mean difference      |
| Point estimate                                                               | -10.42                        |
| Confidence interval                                                          |                               |
| level                                                                        | 95 %                          |
| sides                                                                        | 2-sided                       |
| lower limit                                                                  | -14.17                        |
| upper limit                                                                  | -6.67                         |
| Variability estimate                                                         | Standard error of the mean    |
| Dispersion value                                                             | 1.901                         |

**Secondary: Mean Change From Baseline in Patient Assessment of Pain at Day 169**

|                 |                                                                    |
|-----------------|--------------------------------------------------------------------|
| End point title | Mean Change From Baseline in Patient Assessment of Pain at Day 169 |
|-----------------|--------------------------------------------------------------------|

End point description:

Participants rated the severity of arthritis pain on a 0 to 100 millimeter (mm) Visual Analogue Scale (VAS), where 0 mm = no pain and 100 mm = most severe pain. The mITT population analysis set included all participants in the treatment group corresponding to their randomized treatment group. 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 169

| End point values                     | Placebo              | Mavrilimumab 30 mg    | Mavrilimumab 100 mg   | Mavrilimumab 150 mg   |
|--------------------------------------|----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                   | Reporting group      | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed          | 81                   | 81                    | 85                    | 79                    |
| Units: mm                            |                      |                       |                       |                       |
| arithmetic mean (standard error)     |                      |                       |                       |                       |
| Baseline (n=81, 81, 85, 79)          | 62.16 ( $\pm$ 2.093) | 62.65 ( $\pm$ 2.11)   | 63.58 ( $\pm$ 2.034)  | 62.35 ( $\pm$ 2.217)  |
| Change at Day 169 (n=40, 65, 73, 74) | -15.2 ( $\pm$ 3.006) | -23.14 ( $\pm$ 2.563) | -23.31 ( $\pm$ 2.446) | -26.53 ( $\pm$ 2.483) |

**Statistical analyses**

|                                         |                              |
|-----------------------------------------|------------------------------|
| Statistical analysis title              | Statistical analysis 1       |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 162                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other                        |
| P-value                                 | < 0.045                      |
| Method                                  | Repeated measures model      |
| Parameter estimate                      | Adjusted mean difference     |
| Point estimate                          | -7.94                        |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -15.72                       |
| upper limit                             | -0.17                        |
| Variability estimate                    | Standard error of the mean   |
| Dispersion value                        | 3.95                         |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 3        |
| Comparison groups                       | Placebo v Mavrilimumab 150 mg |
| Number of subjects included in analysis | 160                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 0.004                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted mean difference      |
| Point estimate                          | -11.32                        |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -19                           |
| upper limit                             | -3.65                         |
| Variability estimate                    | Standard error of the mean    |
| Dispersion value                        | 3.899                         |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 2        |
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 166                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 0.037                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted mean difference      |
| Point estimate                          | -8.11                         |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -15.73                        |
| upper limit                             | -0.48                         |
| Variability estimate                    | Standard error of the mean    |
| Dispersion value                        | 3.876                         |

### **Secondary: Mean Change From Baseline in Patient Global Assessment (PGA) of Disease Activity at Day 169**

|                 |                                                                                             |
|-----------------|---------------------------------------------------------------------------------------------|
| End point title | Mean Change From Baseline in Patient Global Assessment (PGA) of Disease Activity at Day 169 |
|-----------------|---------------------------------------------------------------------------------------------|

#### **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 millimeter (mm) VAS, where 0 = very well and 100 = very poorly. The mITT population analysis set included all participants in the treatment group corresponding to their randomized treatment group. 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 169 |           |

| End point values                     | Placebo          | Mavrilimumab 30 mg | Mavrilimumab 100 mg | Mavrilimumab 150 mg |
|--------------------------------------|------------------|--------------------|---------------------|---------------------|
| Subject group type                   | Reporting group  | Reporting group    | Reporting group     | Reporting group     |
| Number of subjects analysed          | 81               | 81                 | 85                  | 79                  |
| Units: mm                            |                  |                    |                     |                     |
| arithmetic mean (standard error)     |                  |                    |                     |                     |
| Baseline (n=81, 81, 85, 79)          | 64.86 (± 1.892)  | 63.79 (± 2.074)    | 63.71 (± 1.957)     | 62.39 (± 2.099)     |
| Change at Day 169 (n=40, 65, 73, 74) | -20.21 (± 3.148) | -21.06 (± 2.685)   | -22.4 (± 2.56)      | -25.69 (± 2.6)      |

### Statistical analyses

|                                         |                              |
|-----------------------------------------|------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 1       |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 162                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other                        |
| P-value                                 | < 0.837                      |
| Method                                  | Repeated measures model      |
| Parameter estimate                      | Adjusted mean difference     |
| Point estimate                          | -0.85                        |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -8.99                        |
| upper limit                             | 7.29                         |
| Variability estimate                    | Standard error of the mean   |
| Dispersion value                        | 4.137                        |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 2        |
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 166                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 0.589                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted mean difference      |
| Point estimate                          | -2.19                         |

|                      |                            |
|----------------------|----------------------------|
| Confidence interval  |                            |
| level                | 95 %                       |
| sides                | 2-sided                    |
| lower limit          | -10.18                     |
| upper limit          | 5.79                       |
| Variability estimate | Standard error of the mean |
| Dispersion value     | 4.058                      |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 3        |
| Comparison groups                       | Placebo v Mavrilimumab 150 mg |
| Number of subjects included in analysis | 160                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 0.18                        |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted mean difference      |
| Point estimate                          | -5.48                         |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -13.52                        |
| upper limit                             | 2.55                          |
| Variability estimate                    | Standard error of the mean    |
| Dispersion value                        | 4.083                         |

### **Secondary: Mean Change From Baseline in Physician Global Assessment of Disease Activity (MDGA) at Day 169**

|                 |                                                                                                |
|-----------------|------------------------------------------------------------------------------------------------|
| End point title | Mean Change From Baseline in Physician Global Assessment of Disease Activity (MDGA) at Day 169 |
|-----------------|------------------------------------------------------------------------------------------------|

#### End point description:

Physician Global Assessment of Arthritis was measured by asking the physician to assess the participant's current arthritis disease activity by placing a vertical line on a 0 to 10 centimeter (cm) VAS, where 0 cm = very good and 10 cm = very bad. The mITT population analysis set included all participants in the treatment group corresponding to their randomized treatment group. 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 169 |           |



| <b>End point values</b>              | Placebo              | Mavrilimumab<br>30 mg | Mavrilimumab<br>100 mg | Mavrilimumab<br>150 mg |
|--------------------------------------|----------------------|-----------------------|------------------------|------------------------|
| Subject group type                   | Reporting group      | Reporting group       | Reporting group        | Reporting group        |
| Number of subjects analysed          | 81                   | 81                    | 85                     | 79                     |
| Units: cm                            |                      |                       |                        |                        |
| arithmetic mean (standard error)     |                      |                       |                        |                        |
| Baseline (n=81, 81, 85, 79)          | 6.6 ( $\pm$ 0.168)   | 6.6 ( $\pm$ 0.162)    | 6.81 ( $\pm$ 0.144)    | 6.42 ( $\pm$ 0.166)    |
| Change at Day 169 (n=40, 65, 73, 74) | -2.39 ( $\pm$ 0.305) | -3.81 ( $\pm$ 0.254)  | -3.85 ( $\pm$ 0.241)   | -3.95 ( $\pm$ 0.243)   |

## Statistical analyses

| <b>Statistical analysis title</b>       | Statistical analysis 1       |
|-----------------------------------------|------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 162                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other                        |
| P-value                                 | < 0.001                      |
| Method                                  | Repeated measures model      |
| Parameter estimate                      | Adjusted mean difference     |
| Point estimate                          | -1.41                        |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -2.2                         |
| upper limit                             | -0.63                        |
| Variability estimate                    | Standard error of the mean   |
| Dispersion value                        | 0.397                        |

| <b>Statistical analysis title</b>       | Statistical analysis 2        |
|-----------------------------------------|-------------------------------|
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 166                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 0.001                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted mean difference      |
| Point estimate                          | -1.46                         |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -2.23                         |
| upper limit                             | -0.69                         |
| Variability estimate                    | Standard error of the mean    |
| Dispersion value                        | 0.389                         |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 3        |
| Comparison groups                       | Placebo v Mavrilimumab 150 mg |
| Number of subjects included in analysis | 160                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 0.001                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted mean difference      |
| Point estimate                          | -1.56                         |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -2.33                         |
| upper limit                             | -0.79                         |
| Variability estimate                    | Standard error of the mean    |
| Dispersion value                        | 0.391                         |

### Secondary: Mean Change from Baseline in Health Assessment Questionnaire Disability Index (HAQ-DI) Score at Day 169

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                         |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Mean Change from Baseline in Health Assessment Questionnaire Disability Index (HAQ-DI) Score at Day 169 |
| 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 was 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 from 0 to 3; where 0 = least difficulty and 3 = extreme difficulty. The mITT population analysis set included all participants in the treatment group corresponding to their randomized treatment group. 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 169                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                         |

| End point values                     | Placebo         | Mavrilimumab 30 mg | Mavrilimumab 100 mg | Mavrilimumab 150 mg |
|--------------------------------------|-----------------|--------------------|---------------------|---------------------|
| Subject group type                   | Reporting group | Reporting group    | Reporting group     | Reporting group     |
| Number of subjects analysed          | 81              | 81                 | 85                  | 79                  |
| Units: units on a scale              |                 |                    |                     |                     |
| arithmetic mean (standard error)     |                 |                    |                     |                     |
| Baseline (n=81, 80, 85, 79)          | 1.63 (± 0.054)  | 1.52 (± 0.07)      | 1.58 (± 0.056)      | 1.58 (± 0.059)      |
| Change at Day 169 (n=40, 65, 73, 74) | -0.29 (± 0.081) | -0.37 (± 0.072)    | -0.46 (± 0.068)     | -0.55 (± 0.069)     |

## Statistical analyses

|                                         |                              |
|-----------------------------------------|------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 1       |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 162                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other                        |
| P-value                                 | < 0.479                      |
| Method                                  | Repeated measures model      |
| Parameter estimate                      | Adjusted mean difference     |
| Point estimate                          | -0.08                        |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -0.29                        |
| upper limit                             | 0.14                         |
| Variability estimate                    | Standard error of the mean   |
| Dispersion value                        | 0.108                        |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 2        |
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 166                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 0.124                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted mean difference      |
| Point estimate                          | -0.16                         |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -0.37                         |
| upper limit                             | 0.04                          |
| Variability estimate                    | Standard error of the mean    |
| Dispersion value                        | 0.106                         |

|                                   |                               |
|-----------------------------------|-------------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 3        |
| Comparison groups                 | Placebo v Mavrilimumab 150 mg |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 160                        |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other                      |
| P-value                                 | < 0.017                    |
| Method                                  | Repeated measures model    |
| Parameter estimate                      | Adjusted mean difference   |
| Point estimate                          | -0.26                      |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | -0.47                      |
| upper limit                             | -0.05                      |
| Variability estimate                    | Standard error of the mean |
| Dispersion value                        | 0.107                      |

### Secondary: Ratio of Change From Baseline in C-Reactive Protein (CRP) at Day 169

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                      |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Ratio of Change From Baseline in C-Reactive Protein (CRP) at Day 169 |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                      |
| CRP is a substance produced by the liver that increases in the presence of inflammation in the body. 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 in underlying disease. The mITT population analysis set included all participants in the treatment group corresponding to their randomized treatment group. Here "N" (Number of participants analyzed) signifies those participants who were evaluable for this measure. |                                                                      |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Secondary                                                            |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                      |
| Baseline, Day 169                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                      |

| End point values                                    | Placebo              | Mavrilimumab 30 mg    | Mavrilimumab 100 mg   | Mavrilimumab 150 mg   |
|-----------------------------------------------------|----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                                  | Reporting group      | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed                         | 38                   | 63                    | 72                    | 74                    |
| Units: ratio                                        |                      |                       |                       |                       |
| geometric mean (geometric coefficient of variation) | 1.2971 ( $\pm$ 83.3) | 0.8784 ( $\pm$ 102.8) | 0.5197 ( $\pm$ 287.4) | 0.5856 ( $\pm$ 153.3) |

### Statistical analyses

|                            |                              |
|----------------------------|------------------------------|
| Statistical analysis title | Statistical analysis 1       |
| Comparison groups          | Placebo v Mavrilimumab 30 mg |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| Number of subjects included in analysis | 101                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 0.017                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted geometric mean ratio |
| Point estimate                          | 0.64                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 0.45                          |
| upper limit                             | 0.92                          |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 3        |
| Comparison groups                       | Placebo v Mavrilimumab 150 mg |
| Number of subjects included in analysis | 112                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 0.001                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted geometric mean ratio |
| Point estimate                          | 0.44                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 0.31                          |
| upper limit                             | 0.63                          |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 2        |
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 110                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 0.001                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted geometric mean ratio |
| Point estimate                          | 0.46                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 0.32                          |
| upper limit                             | 0.66                          |

---

## Secondary: Ratio of Change From Baseline in Erythrocyte Sedimentation Rate (ESR)

---

**at Day 169**

|                 |                                                                                  |
|-----------------|----------------------------------------------------------------------------------|
| End point title | Ratio of Change From Baseline in Erythrocyte Sedimentation Rate (ESR) at Day 169 |
|-----------------|----------------------------------------------------------------------------------|

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 farther the red blood cells have descended, the greater the inflammatory response. The mITT population analysis set included all participants in the treatment group corresponding to their randomized treatment group. Here "N" (Number of participants analyzed) signifies those participants who were evaluable for this measure.

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

End point timeframe:

Baseline, Day 169

| <b>End point values</b>                             | Placebo         | Mavrilimumab 30 mg | Mavrilimumab 100 mg | Mavrilimumab 150 mg |
|-----------------------------------------------------|-----------------|--------------------|---------------------|---------------------|
| Subject group type                                  | Reporting group | Reporting group    | Reporting group     | Reporting group     |
| Number of subjects analysed                         | 40              | 64                 | 73                  | 74                  |
| Units: ratio                                        |                 |                    |                     |                     |
| geometric mean (geometric coefficient of variation) | 0.89 (± 57)     | 0.67 (± 56.4)      | 0.62 (± 55.3)       | 0.58 (± 61)         |

**Statistical analyses**

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 1        |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg  |
| Number of subjects included in analysis | 104                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 0.003                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted geometric mean ratio |
| Point estimate                          | 0.72                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 0.58                          |
| upper limit                             | 0.89                          |

|                                   |                               |
|-----------------------------------|-------------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 2        |
| Comparison groups                 | Placebo v Mavrilimumab 100 mg |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| Number of subjects included in analysis | 113                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 0.001                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted geometric mean ratio |
| Point estimate                          | 0.68                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 0.55                          |
| upper limit                             | 0.84                          |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 3        |
| Comparison groups                       | Placebo v Mavrilimumab 150 mg |
| Number of subjects included in analysis | 114                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 0.001                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted geometric mean ratio |
| Point estimate                          | 0.61                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 0.49                          |
| upper limit                             | 0.75                          |

### **Secondary: Percentage of Participants With Simplified Disease Activity Index (SDAI) Remission at Day 169**

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                               |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Percentage of Participants With Simplified Disease Activity Index (SDAI) Remission at Day 169 |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                               |
| <p>The SDAI was the numerical sum of five outcome parameters: TJC and SJC based on a 28-joint assessment, patient global assessment and physician global assessment assessed on 0 - 10 cm VAS; and C-reactive protein (CRP) (milligram per deciliter [mg/dL]). The SDAI total score ranges from 0 to 86, where higher scores indicates greater affection due to disease activity. SDAI remission was defined as a score less than or equal to 3.3. The mITT population analysis set included all participants in the treatment group corresponding to their randomized treatment group.</p> |                                                                                               |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Secondary                                                                                     |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                               |
| Day 169                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                               |

| <b>End point values</b>           | Placebo         | Mavrilimumab<br>30 mg | Mavrilimumab<br>100 mg | Mavrilimumab<br>150 mg |
|-----------------------------------|-----------------|-----------------------|------------------------|------------------------|
| Subject group type                | Reporting group | Reporting group       | Reporting group        | Reporting group        |
| Number of subjects analysed       | 81              | 81                    | 85                     | 79                     |
| Units: percentage of participants |                 |                       |                        |                        |
| number (not applicable)           | 1.2             | 6.2                   | 2.4                    | 5.1                    |

## Statistical analyses

|                                         |                              |
|-----------------------------------------|------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 1       |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 162                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other                        |
| P-value                                 | < 0.21                       |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 4.9                          |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -0.8                         |
| upper limit                             | 10.7                         |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 2        |
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 166                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 1                           |
| Method                                  | Fisher exact                  |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | 1.1                           |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -2.9                          |
| upper limit                             | 5.1                           |

|                                   |                               |
|-----------------------------------|-------------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 3        |
| Comparison groups                 | Placebo v Mavrilimumab 150 mg |



|                                         |                    |
|-----------------------------------------|--------------------|
| Number of subjects included in analysis | 160                |
| Analysis specification                  | Pre-specified      |
| Analysis type                           | other              |
| P-value                                 | < 0.207            |
| Method                                  | Fisher exact       |
| Parameter estimate                      | Percent difference |
| Point estimate                          | 3.8                |
| Confidence interval                     |                    |
| level                                   | 95 %               |
| sides                                   | 2-sided            |
| lower limit                             | -1.6               |
| upper limit                             | 9.2                |

### Secondary: Percentage of Participants With Clinical Disease Activity Index (CDAI) Remission at Day 169

|                 |                                                                                             |
|-----------------|---------------------------------------------------------------------------------------------|
| End point title | Percentage of Participants With Clinical Disease Activity Index (CDAI) Remission at Day 169 |
|-----------------|---------------------------------------------------------------------------------------------|

End point description:

The CDAI was the numerical sum of 4 outcome parameters: TJC and SJC based on a 28-joint assessment, patient global assessment and physician global assessment assessed on 0 - 10 cm VAS. The CDAI total score ranges from 0 to 76 where higher scores indicates greater affection due to disease activity. CDAI remission was defined as a score less than or equal to 2.8. The mITT population analysis set included all participants in the treatment group corresponding to their randomized treatment group.

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

End point timeframe:

Day 169

| End point values                  | Placebo         | Mavrilimumab 30 mg | Mavrilimumab 100 mg | Mavrilimumab 150 mg |
|-----------------------------------|-----------------|--------------------|---------------------|---------------------|
| Subject group type                | Reporting group | Reporting group    | Reporting group     | Reporting group     |
| Number of subjects analysed       | 81              | 81                 | 85                  | 79                  |
| Units: percentage of participants |                 |                    |                     |                     |
| number (not applicable)           | 1.2             | 6.2                | 3.5                 | 7.6                 |

### Statistical analyses

|                                         |                              |
|-----------------------------------------|------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 1       |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 162                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other                        |
| P-value                                 | < 0.21                       |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 4.9                          |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -0.8    |
| upper limit         | 10.7    |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 2        |
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 166                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 0.621                       |
| Method                                  | Fisher exact                  |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | 2.3                           |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -2.3                          |
| upper limit                             | 6.9                           |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 3        |
| Comparison groups                       | Placebo v Mavrilimumab 150 mg |
| Number of subjects included in analysis | 160                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 0.062                       |
| Method                                  | Fisher exact                  |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | 6.4                           |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 0                             |
| upper limit                             | 12.7                          |

### **Secondary: Percentage of Participants With American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) Remission at Day 169**

|                 |                                                                                                                                      |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Participants With American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) Remission at Day 169 |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------|

End point description:

ACR/EULAR remission was defined as swollen joint count (0-66), tender joint count (0-68), CRP (mg/dL) and participant global assessment (0-10) all less than or equal to one. The mITT population analysis set

included all participants in the treatment group corresponding to their randomized treatment group.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Day 169              |           |

| End point values                  | Placebo         | Mavrilimumab<br>30 mg | Mavrilimumab<br>100 mg | Mavrilimumab<br>150 mg |
|-----------------------------------|-----------------|-----------------------|------------------------|------------------------|
| Subject group type                | Reporting group | Reporting group       | Reporting group        | Reporting group        |
| Number of subjects analysed       | 81              | 81                    | 85                     | 79                     |
| Units: percentage of participants |                 |                       |                        |                        |
| number (not applicable)           | 0               | 3.7                   | 1.2                    | 1.3                    |

### Statistical analyses

|                                         |                              |
|-----------------------------------------|------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 1       |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 162                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other                        |
| P-value                                 | < 0.245                      |
| Method                                  | Fisher exact                 |
| Parameter estimate                      | Percent difference           |
| Point estimate                          | 3.7                          |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -0.4                         |
| upper limit                             | 7.8                          |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 2        |
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 166                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 1                           |
| Method                                  | Fisher exact                  |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | 1.2                           |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -1.1                          |
| upper limit                             | 3.5                           |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 3        |
| Comparison groups                       | Placebo v Mavrilimumab 150 mg |
| Number of subjects included in analysis | 160                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 0.494                       |
| Method                                  | Fisher exact                  |
| Parameter estimate                      | Percent difference            |
| Point estimate                          | 1.3                           |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -1.2                          |
| upper limit                             | 3.7                           |

### Secondary: Mean Change From Baseline in Functional Assessment of Chronic Illness Therapy-fatigue (FACIT-fatigue) at Day 169

|                 |                                                                                                                  |
|-----------------|------------------------------------------------------------------------------------------------------------------|
| End point title | Mean Change From Baseline in Functional Assessment of Chronic Illness Therapy-fatigue (FACIT-fatigue) at Day 169 |
|-----------------|------------------------------------------------------------------------------------------------------------------|

End point description:

FACIT-F is a 13-item questionnaire to measure the degree of fatigue experiences by participants in the previous 7 days. Participants scored each item on a 5-point scale: 0 (not at all) to 4 (very much). Larger the participant's response to the questions (with the exception of 2 negatively stated), greater was the participant's fatigue. For all questions, except for the 2 negatively stated ones, the code was reversed and a new score was calculated as (4 minus the participant's response). The sum of all responses resulted in the FACIT-Fatigue score for a total possible score of 0 (worse score) to 52 (better score) where higher score represent less fatigue. The mITT population analysis set included all participants in the treatment group corresponding to their randomized treatment group. 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 169

| <b>End point values</b>              | Placebo         | Mavrilimumab 30 mg | Mavrilimumab 100 mg | Mavrilimumab 150 mg |
|--------------------------------------|-----------------|--------------------|---------------------|---------------------|
| Subject group type                   | Reporting group | Reporting group    | Reporting group     | Reporting group     |
| Number of subjects analysed          | 81              | 81                 | 85                  | 79                  |
| Units: units on a scale              |                 |                    |                     |                     |
| arithmetic mean (standard error)     |                 |                    |                     |                     |
| Baseline (n=79, 80, 84, 79)          | 26.75 (± 0.824) | 28.91 (± 1.078)    | 28.45 (± 0.998)     | 27.82 (± 0.95)      |
| Change at Day 169 (n=40, 65, 73, 74) | 4.53 (± 1.225)  | 5.72 (± 1.039)     | 6.8 (± 0.988)       | 8.45 (± 0.997)      |

## Statistical analyses

|                                         |                              |
|-----------------------------------------|------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 1       |
| Comparison groups                       | Placebo v Mavrilimumab 30 mg |
| Number of subjects included in analysis | 162                          |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | other                        |
| P-value                                 | < 0.463                      |
| Method                                  | Repeated measures model      |
| Parameter estimate                      | Adjusted mean difference     |
| Point estimate                          | 1.18                         |
| Confidence interval                     |                              |
| level                                   | 95 %                         |
| sides                                   | 2-sided                      |
| lower limit                             | -1.99                        |
| upper limit                             | 4.35                         |
| Variability estimate                    | Standard error of the mean   |
| Dispersion value                        | 1.608                        |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 2        |
| Comparison groups                       | Placebo v Mavrilimumab 100 mg |
| Number of subjects included in analysis | 166                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 0.151                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted mean difference      |
| Point estimate                          | 2.27                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | -0.83                         |
| upper limit                             | 5.37                          |
| Variability estimate                    | Standard error of the mean    |
| Dispersion value                        | 1.574                         |

|                                         |                               |
|-----------------------------------------|-------------------------------|
| <b>Statistical analysis title</b>       | Statistical analysis 3        |
| Comparison groups                       | Placebo v Mavrilimumab 150 mg |
| Number of subjects included in analysis | 160                           |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           | other                         |
| P-value                                 | < 0.014                       |
| Method                                  | Repeated measures model       |
| Parameter estimate                      | Adjusted mean difference      |
| Point estimate                          | 3.92                          |

|                      |                            |
|----------------------|----------------------------|
| Confidence interval  |                            |
| level                | 95 %                       |
| sides                | 2-sided                    |
| lower limit          | 0.81                       |
| upper limit          | 7.02                       |
| Variability estimate | Standard error of the mean |
| Dispersion value     | 1.578                      |

## Secondary: Serum Concentrations of Mavrilimumab

|                 |                                                     |
|-----------------|-----------------------------------------------------|
| End point title | Serum Concentrations of Mavrilimumab <sup>[1]</sup> |
|-----------------|-----------------------------------------------------|

End point description:

Serum concentrations after multiple subcutaneous doses of mavrilimumab were calculated for each cohort (30mg, 100mg and 150mg). In the below table, '99999' indicates data was not reported for the geometric coefficient of variation for the respective timepoint. 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 the specified time point for each arm, respectively.

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

End point timeframe:

Baseline, Day 8, 15, 29, 85, 141, and 169

Notes:

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

Justification: Placebo-treated subjects (N=81) were excluded from the pharmacokinetic analysis.

| End point values                                    | Mavrilimumab<br>30 mg | Mavrilimumab<br>100 mg | Mavrilimumab<br>150 mg |  |
|-----------------------------------------------------|-----------------------|------------------------|------------------------|--|
| Subject group type                                  | Reporting group       | Reporting group        | Reporting group        |  |
| Number of subjects analysed                         | 81                    | 85                     | 79                     |  |
| Units: nanogram per milliliter                      |                       |                        |                        |  |
| geometric mean (geometric coefficient of variation) |                       |                        |                        |  |
| Baseline (n=80, 85, 79)                             | 0 (± 894.4)           | 0 (± 99999)            | 0 (± 862)              |  |
| Day 8 (n=78, 83, 78)                                | 617.49 (± 111.8)      | 3563.31 (± 49.3)       | 6087.06 (± 43.4)       |  |
| Day 15 (n=78, 84, 78)                               | 154.6 (± 194.2)       | 2479.96 (± 52.1)       | 4616.35 (± 42.6)       |  |
| Day 29 (n=77, 85, 76)                               | 217.67 (± 248.3)      | 4503.97 (± 54.8)       | 7843.66 (± 42.9)       |  |
| Day 85 (n=74, 81, 77)                               | 201.57 (± 162.8)      | 6538.22 (± 52.7)       | 13213.93 (± 50.1)      |  |
| Day 141 (n=67, 75, 71)                              | 258.77 (± 136.9)      | 2932.8 (± 75.6)        | 9241.31 (± 52.1)       |  |
| Day 169 (n=63, 73, 74)                              | 348.97 (± 141.2)      | 5282.37 (± 62)         | 9178.47 (± 56.6)       |  |

## Statistical analyses

No statistical analyses for this end point

---

**Secondary: Percentage of Participants Exhibiting Anti-Drug Antibodies (ADAs) to Mavrilimumab at any Visit**

---

|                 |                                                                                                |
|-----------------|------------------------------------------------------------------------------------------------|
| End point title | Percentage of Participants Exhibiting Anti-Drug Antibodies (ADAs) to Mavrilimumab at any Visit |
|-----------------|------------------------------------------------------------------------------------------------|

End point description:

Immunogenicity assessment included determination of anti-drug (mavrilimumab) antibodies in serum samples. ADA detection measured by using electrochemiluminescence assays. The immunogenicity population included all participants who received at least 1 dose of mavrilimumab and for whom at least one serum sample for immunogenicity testing was available.

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

End point timeframe:

Day 1 to Day 169

---

| End point values                  | Placebo         | Mavrilimumab 30 mg | Mavrilimumab 100 mg | Mavrilimumab 150 mg |
|-----------------------------------|-----------------|--------------------|---------------------|---------------------|
| Subject group type                | Reporting group | Reporting group    | Reporting group     | Reporting group     |
| Number of subjects analysed       | 81              | 81                 | 85                  | 79                  |
| Units: percentage of participants |                 |                    |                     |                     |
| number (not applicable)           | 2.5             | 16                 | 3.5                 | 0                   |

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**Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline up to Day 169

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 16.1 |
|--------------------|------|

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | PLACEBO |
|-----------------------|---------|

Reporting group description: -

|                       |                    |
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| Reporting group title | MAVRILIMUMAB 100MG |
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Reporting group description: -

|                       |                    |
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| Reporting group title | MAVRILIMUMAB 150MG |
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Reporting group description: -

|                       |                   |
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| Reporting group title | MAVRILIMUMAB 30MG |
|-----------------------|-------------------|

Reporting group description: -

| Serious adverse events                                              | PLACEBO        | MAVRILIMUMAB 100MG | MAVRILIMUMAB 150MG |
|---------------------------------------------------------------------|----------------|--------------------|--------------------|
| Total subjects affected by serious adverse events                   |                |                    |                    |
| subjects affected / exposed                                         | 1 / 81 (1.23%) | 5 / 85 (5.88%)     | 2 / 79 (2.53%)     |
| number of deaths (all causes)                                       | 0              | 0                  | 0                  |
| number of deaths resulting from adverse events                      | 0              | 0                  | 0                  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                |                    |                    |
| Adenocarcinoma of the cervix                                        |                |                    |                    |
| subjects affected / exposed                                         | 0 / 81 (0.00%) | 1 / 85 (1.18%)     | 0 / 79 (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              |
| Squamous cell carcinoma of lung                                     |                |                    |                    |
| subjects affected / exposed                                         | 0 / 81 (0.00%) | 0 / 85 (0.00%)     | 1 / 79 (1.27%)     |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0              | 0 / 1              |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0              | 0 / 0              |
| Injury, poisoning and procedural complications                      |                |                    |                    |
| Lower limb fracture                                                 |                |                    |                    |
| subjects affected / exposed                                         | 0 / 81 (0.00%) | 0 / 85 (0.00%)     | 0 / 79 (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              |



|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Tendon rupture                                  |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 85 (1.18%) | 0 / 79 (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          |
| Cardiac disorders                               |                |                |                |
| Atrial tachycardia                              |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 85 (1.18%) | 0 / 79 (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          |
| Supraventricular tachycardia                    |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 85 (1.18%) | 0 / 79 (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          |
| Gastrointestinal disorders                      |                |                |                |
| Dyspepsia                                       |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 85 (1.18%) | 0 / 79 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Reproductive system and breast disorders        |                |                |                |
| Cystocele                                       |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 0 / 79 (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          |
| Hepatobiliary disorders                         |                |                |                |
| Cholelithiasis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 85 (1.18%) | 0 / 79 (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          |
| Skin and subcutaneous tissue disorders          |                |                |                |
| Angioedema                                      |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal and connective tissue disorders |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Osteoarthritis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 0 / 79 (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          |
| Rheumatoid arthritis                            |                |                |                |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 0 / 85 (0.00%) | 0 / 79 (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          |
| Infections and infestations                     |                |                |                |
| Pneumonia                                       |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 0 / 79 (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          |

| Serious adverse events                                              | MAVRILIMUMAB<br>30MG |  |  |
|---------------------------------------------------------------------|----------------------|--|--|
| Total subjects affected by serious adverse events                   |                      |  |  |
| subjects affected / exposed                                         | 4 / 81 (4.94%)       |  |  |
| number of deaths (all causes)                                       | 0                    |  |  |
| number of deaths resulting from adverse events                      | 0                    |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                      |  |  |
| Adenocarcinoma of the cervix                                        |                      |  |  |
| subjects affected / exposed                                         | 0 / 81 (0.00%)       |  |  |
| occurrences causally related to treatment / all                     | 0 / 0                |  |  |
| deaths causally related to treatment / all                          | 0 / 0                |  |  |
| Squamous cell carcinoma of lung                                     |                      |  |  |
| subjects affected / exposed                                         | 0 / 81 (0.00%)       |  |  |
| occurrences causally related to treatment / all                     | 0 / 0                |  |  |
| deaths causally related to treatment / all                          | 0 / 0                |  |  |
| Injury, poisoning and procedural complications                      |                      |  |  |
| Lower limb fracture                                                 |                      |  |  |
| subjects affected / exposed                                         | 1 / 81 (1.23%)       |  |  |
| occurrences causally related to treatment / all                     | 0 / 1                |  |  |
| deaths causally related to treatment / all                          | 0 / 0                |  |  |
| Tendon rupture                                                      |                      |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Cardiac disorders                               |                |  |  |
| Atrial tachycardia                              |                |  |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Supraventricular tachycardia                    |                |  |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Gastrointestinal disorders                      |                |  |  |
| Dyspepsia                                       |                |  |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Reproductive system and breast disorders        |                |  |  |
| Cystocele                                       |                |  |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Hepatobiliary disorders                         |                |  |  |
| Cholelithiasis                                  |                |  |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Skin and subcutaneous tissue disorders          |                |  |  |
| Angioedema                                      |                |  |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Musculoskeletal and connective tissue disorders |                |  |  |
| Osteoarthritis                                  |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 1 / 81 (1.23%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Rheumatoid arthritis                            |                |  |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Infections and infestations                     |                |  |  |
| Pneumonia                                       |                |  |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

Frequency threshold for reporting non-serious adverse events: 0 %

| <b>Non-serious adverse events</b>                     | PLACEBO          | MAVRILIMUMAB<br>100MG | MAVRILIMUMAB<br>150MG |
|-------------------------------------------------------|------------------|-----------------------|-----------------------|
| Total subjects affected by non-serious adverse events |                  |                       |                       |
| subjects affected / exposed                           | 38 / 81 (46.91%) | 33 / 85 (38.82%)      | 42 / 79 (53.16%)      |
| Vascular disorders                                    |                  |                       |                       |
| Haematoma                                             |                  |                       |                       |
| subjects affected / exposed                           | 0 / 81 (0.00%)   | 0 / 85 (0.00%)        | 0 / 79 (0.00%)        |
| occurrences (all)                                     | 0                | 0                     | 0                     |
| Hot flush                                             |                  |                       |                       |
| subjects affected / exposed                           | 0 / 81 (0.00%)   | 1 / 85 (1.18%)        | 0 / 79 (0.00%)        |
| occurrences (all)                                     | 0                | 1                     | 0                     |
| Hypertension                                          |                  |                       |                       |
| subjects affected / exposed                           | 2 / 81 (2.47%)   | 4 / 85 (4.71%)        | 3 / 79 (3.80%)        |
| occurrences (all)                                     | 2                | 5                     | 3                     |
| Venous insufficiency                                  |                  |                       |                       |
| subjects affected / exposed                           | 1 / 81 (1.23%)   | 0 / 85 (0.00%)        | 0 / 79 (0.00%)        |
| occurrences (all)                                     | 1                | 0                     | 0                     |
| General disorders and administration site conditions  |                  |                       |                       |
| Fatigue                                               |                  |                       |                       |
| subjects affected / exposed                           | 0 / 81 (0.00%)   | 0 / 85 (0.00%)        | 0 / 79 (0.00%)        |
| occurrences (all)                                     | 0                | 0                     | 0                     |

|                                          |                |                |                |
|------------------------------------------|----------------|----------------|----------------|
| Feeling hot                              |                |                |                |
| subjects affected / exposed              | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)                        | 0              | 0              | 1              |
| Influenza like illness                   |                |                |                |
| subjects affected / exposed              | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)                        | 0              | 0              | 1              |
| Injection site erythema                  |                |                |                |
| subjects affected / exposed              | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)                        | 0              | 0              | 3              |
| Injection site haematoma                 |                |                |                |
| subjects affected / exposed              | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)                        | 0              | 0              | 1              |
| Injection site swelling                  |                |                |                |
| subjects affected / exposed              | 1 / 81 (1.23%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)                        | 1              | 0              | 2              |
| Injection site reaction                  |                |                |                |
| subjects affected / exposed              | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)                        | 0              | 0              | 1              |
| Oedema peripheral                        |                |                |                |
| subjects affected / exposed              | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 0 / 79 (0.00%) |
| occurrences (all)                        | 0              | 0              | 0              |
| Pyrexia                                  |                |                |                |
| subjects affected / exposed              | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 0 / 79 (0.00%) |
| occurrences (all)                        | 0              | 0              | 0              |
| Immune system disorders                  |                |                |                |
| Allergy to arthropod bite                |                |                |                |
| subjects affected / exposed              | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)                        | 0              | 0              | 1              |
| Drug hypersensitivity                    |                |                |                |
| subjects affected / exposed              | 1 / 81 (1.23%) | 0 / 85 (0.00%) | 2 / 79 (2.53%) |
| occurrences (all)                        | 1              | 0              | 2              |
| Hypersensitivity                         |                |                |                |
| subjects affected / exposed              | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 0 / 79 (0.00%) |
| occurrences (all)                        | 0              | 0              | 0              |
| Reproductive system and breast disorders |                |                |                |

|                                                                                           |                     |                     |                     |
|-------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Cervical dysplasia<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 81 (1.23%)<br>1 | 0 / 85 (0.00%)<br>0 | 0 / 79 (0.00%)<br>0 |
| Endometriosis<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 81 (0.00%)<br>0 | 1 / 85 (1.18%)<br>1 | 0 / 79 (0.00%)<br>0 |
| Uterine polyp<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 81 (0.00%)<br>0 | 1 / 85 (1.18%)<br>1 | 0 / 79 (0.00%)<br>0 |
| Vaginal discharge<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 81 (0.00%)<br>0 | 1 / 85 (1.18%)<br>1 | 0 / 79 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal disorders                                           |                     |                     |                     |
| Bronchiectasis<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 81 (0.00%)<br>0 | 1 / 85 (1.18%)<br>1 | 0 / 79 (0.00%)<br>0 |
| Bronchospasm<br>subjects affected / exposed<br>occurrences (all)                          | 1 / 81 (1.23%)<br>1 | 0 / 85 (0.00%)<br>0 | 0 / 79 (0.00%)<br>0 |
| Chronic obstructive pulmonary disease<br>subjects affected / exposed<br>occurrences (all) | 0 / 81 (0.00%)<br>0 | 0 / 85 (0.00%)<br>0 | 0 / 79 (0.00%)<br>0 |
| Cough<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 81 (0.00%)<br>0 | 1 / 85 (1.18%)<br>1 | 0 / 79 (0.00%)<br>0 |
| Obstructive airways disorder<br>subjects affected / exposed<br>occurrences (all)          | 0 / 81 (0.00%)<br>0 | 0 / 85 (0.00%)<br>0 | 1 / 79 (1.27%)<br>1 |
| Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 81 (0.00%)<br>0 | 0 / 85 (0.00%)<br>0 | 1 / 79 (1.27%)<br>1 |
| Pleural effusion<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 81 (1.23%)<br>1 | 0 / 85 (0.00%)<br>0 | 0 / 79 (0.00%)<br>0 |
| Pulmonary mass                                                                            |                     |                     |                     |

|                                                                                          |                     |                     |                     |
|------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                         | 0 / 81 (0.00%)<br>0 | 0 / 85 (0.00%)<br>0 | 1 / 79 (1.27%)<br>1 |
| Rhinorrhoea<br>subjects affected / exposed<br>occurrences (all)                          | 1 / 81 (1.23%)<br>2 | 0 / 85 (0.00%)<br>0 | 0 / 79 (0.00%)<br>0 |
| Psychiatric disorders                                                                    |                     |                     |                     |
| Anxiety<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 81 (0.00%)<br>0 | 1 / 85 (1.18%)<br>1 | 0 / 79 (0.00%)<br>0 |
| Depression<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 81 (0.00%)<br>0 | 0 / 85 (0.00%)<br>0 | 1 / 79 (1.27%)<br>1 |
| Dyssomnia<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 81 (0.00%)<br>0 | 0 / 85 (0.00%)<br>0 | 1 / 79 (1.27%)<br>1 |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 81 (0.00%)<br>0 | 1 / 85 (1.18%)<br>1 | 0 / 79 (0.00%)<br>0 |
| Investigations                                                                           |                     |                     |                     |
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)   | 0 / 81 (0.00%)<br>0 | 1 / 85 (1.18%)<br>1 | 1 / 79 (1.27%)<br>1 |
| Aspartate aminotransferase increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 81 (0.00%)<br>0 | 1 / 85 (1.18%)<br>1 | 0 / 79 (0.00%)<br>0 |
| Blood pressure increased<br>subjects affected / exposed<br>occurrences (all)             | 1 / 81 (1.23%)<br>2 | 0 / 85 (0.00%)<br>0 | 0 / 79 (0.00%)<br>0 |
| Gamma-glutamyltransferase increased<br>subjects affected / exposed<br>occurrences (all)  | 0 / 81 (0.00%)<br>0 | 0 / 85 (0.00%)<br>0 | 0 / 79 (0.00%)<br>0 |
| Weight increased<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 81 (1.23%)<br>1 | 1 / 85 (1.18%)<br>1 | 0 / 79 (0.00%)<br>0 |
| Injury, poisoning and procedural complications                                           |                     |                     |                     |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Alcohol poisoning           |                |                |                |
| subjects affected / exposed | 0 / 81 (0.00%) | 1 / 85 (1.18%) | 0 / 79 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Animal bite                 |                |                |                |
| subjects affected / exposed | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 0 / 79 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Bone contusion              |                |                |                |
| subjects affected / exposed | 1 / 81 (1.23%) | 0 / 85 (0.00%) | 0 / 79 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Chemical poisoning          |                |                |                |
| subjects affected / exposed | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 0 / 79 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Clavicle fracture           |                |                |                |
| subjects affected / exposed | 1 / 81 (1.23%) | 0 / 85 (0.00%) | 0 / 79 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Contusion                   |                |                |                |
| subjects affected / exposed | 1 / 81 (1.23%) | 1 / 85 (1.18%) | 0 / 79 (0.00%) |
| occurrences (all)           | 1              | 1              | 0              |
| Epicondylitis               |                |                |                |
| subjects affected / exposed | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 0 / 79 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Fall                        |                |                |                |
| subjects affected / exposed | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)           | 0              | 0              | 1              |
| Injection related reaction  |                |                |                |
| subjects affected / exposed | 0 / 81 (0.00%) | 1 / 85 (1.18%) | 0 / 79 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Laceration                  |                |                |                |
| subjects affected / exposed | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)           | 0              | 0              | 1              |
| Limb injury                 |                |                |                |
| subjects affected / exposed | 0 / 81 (0.00%) | 2 / 85 (2.35%) | 0 / 79 (0.00%) |
| occurrences (all)           | 0              | 2              | 0              |
| Muscle contusion            |                |                |                |
| subjects affected / exposed | 0 / 81 (0.00%) | 1 / 85 (1.18%) | 1 / 79 (1.27%) |
| occurrences (all)           | 0              | 1              | 1              |



|                                                                                  |                     |                     |                     |
|----------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Cardiac disorders                                                                |                     |                     |                     |
| Arrhythmia supraventricular<br>subjects affected / exposed<br>occurrences (all)  | 0 / 81 (0.00%)<br>0 | 1 / 85 (1.18%)<br>1 | 0 / 79 (0.00%)<br>0 |
| Cardiac failure<br>subjects affected / exposed<br>occurrences (all)              | 1 / 81 (1.23%)<br>1 | 0 / 85 (0.00%)<br>0 | 0 / 79 (0.00%)<br>0 |
| Cardiovascular insufficiency<br>subjects affected / exposed<br>occurrences (all) | 1 / 81 (1.23%)<br>1 | 0 / 85 (0.00%)<br>0 | 0 / 79 (0.00%)<br>0 |
| Nervous system disorders                                                         |                     |                     |                     |
| Headache<br>subjects affected / exposed<br>occurrences (all)                     | 2 / 81 (2.47%)<br>2 | 4 / 85 (4.71%)<br>4 | 6 / 79 (7.59%)<br>8 |
| Intercostal neuralgia<br>subjects affected / exposed<br>occurrences (all)        | 0 / 81 (0.00%)<br>0 | 1 / 85 (1.18%)<br>1 | 0 / 79 (0.00%)<br>0 |
| Sciatica<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 81 (0.00%)<br>0 | 0 / 85 (0.00%)<br>0 | 1 / 79 (1.27%)<br>1 |
| Blood and lymphatic system disorders                                             |                     |                     |                     |
| Anaemia<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 81 (1.23%)<br>1 | 0 / 85 (0.00%)<br>0 | 0 / 79 (0.00%)<br>0 |
| Eosinophilia<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 81 (0.00%)<br>0 | 1 / 85 (1.18%)<br>1 | 0 / 79 (0.00%)<br>0 |
| Leukocytosis<br>subjects affected / exposed<br>occurrences (all)                 | 2 / 81 (2.47%)<br>2 | 0 / 85 (0.00%)<br>0 | 0 / 79 (0.00%)<br>0 |
| Lymphopenia<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 81 (0.00%)<br>0 | 0 / 85 (0.00%)<br>0 | 1 / 79 (1.27%)<br>1 |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 81 (1.23%)<br>1 | 0 / 85 (0.00%)<br>0 | 3 / 79 (3.80%)<br>4 |
| Ear and labyrinth disorders                                                      |                     |                     |                     |

|                                                                              |                     |                     |                     |
|------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Vertigo<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 81 (0.00%)<br>0 | 1 / 85 (1.18%)<br>1 | 0 / 79 (0.00%)<br>0 |
| Eye disorders                                                                |                     |                     |                     |
| Conjunctival haemorrhage<br>subjects affected / exposed<br>occurrences (all) | 0 / 81 (0.00%)<br>0 | 0 / 85 (0.00%)<br>0 | 1 / 79 (1.27%)<br>1 |
| Conjunctivitis<br>subjects affected / exposed<br>occurrences (all)           | 0 / 81 (0.00%)<br>0 | 2 / 85 (2.35%)<br>2 | 0 / 79 (0.00%)<br>0 |
| Keratitis<br>subjects affected / exposed<br>occurrences (all)                | 0 / 81 (0.00%)<br>0 | 1 / 85 (1.18%)<br>1 | 0 / 79 (0.00%)<br>0 |
| Gastrointestinal disorders                                                   |                     |                     |                     |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)           | 1 / 81 (1.23%)<br>1 | 0 / 85 (0.00%)<br>0 | 1 / 79 (1.27%)<br>1 |
| Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)     | 1 / 81 (1.23%)<br>1 | 0 / 85 (0.00%)<br>0 | 0 / 79 (0.00%)<br>0 |
| Cheilitis<br>subjects affected / exposed<br>occurrences (all)                | 0 / 81 (0.00%)<br>0 | 1 / 85 (1.18%)<br>1 | 0 / 79 (0.00%)<br>0 |
| Constipation<br>subjects affected / exposed<br>occurrences (all)             | 1 / 81 (1.23%)<br>1 | 0 / 85 (0.00%)<br>0 | 0 / 79 (0.00%)<br>0 |
| Dental caries<br>subjects affected / exposed<br>occurrences (all)            | 0 / 81 (0.00%)<br>0 | 1 / 85 (1.18%)<br>1 | 1 / 79 (1.27%)<br>1 |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                | 0 / 81 (0.00%)<br>0 | 0 / 85 (0.00%)<br>0 | 2 / 79 (2.53%)<br>2 |
| Dyspepsia<br>subjects affected / exposed<br>occurrences (all)                | 1 / 81 (1.23%)<br>1 | 1 / 85 (1.18%)<br>1 | 0 / 79 (0.00%)<br>0 |
| Gastritis                                                                    |                     |                     |                     |

|                                        |                |                |                |
|----------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed            | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 2 / 79 (2.53%) |
| occurrences (all)                      | 0              | 0              | 2              |
| Gingival swelling                      |                |                |                |
| subjects affected / exposed            | 0 / 81 (0.00%) | 1 / 85 (1.18%) | 0 / 79 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0              |
| Haemorrhoids                           |                |                |                |
| subjects affected / exposed            | 1 / 81 (1.23%) | 0 / 85 (0.00%) | 0 / 79 (0.00%) |
| occurrences (all)                      | 1              | 0              | 0              |
| Irritable bowel syndrome               |                |                |                |
| subjects affected / exposed            | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)                      | 0              | 0              | 1              |
| Mouth cyst                             |                |                |                |
| subjects affected / exposed            | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)                      | 0              | 0              | 1              |
| Nausea                                 |                |                |                |
| subjects affected / exposed            | 1 / 81 (1.23%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)                      | 1              | 0              | 1              |
| Vomiting                               |                |                |                |
| subjects affected / exposed            | 0 / 81 (0.00%) | 1 / 85 (1.18%) | 0 / 79 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0              |
| Hepatobiliary disorders                |                |                |                |
| Hypertransaminasaemia                  |                |                |                |
| subjects affected / exposed            | 0 / 81 (0.00%) | 2 / 85 (2.35%) | 2 / 79 (2.53%) |
| occurrences (all)                      | 0              | 2              | 2              |
| Skin and subcutaneous tissue disorders |                |                |                |
| Dermatitis atopic                      |                |                |                |
| subjects affected / exposed            | 0 / 81 (0.00%) | 1 / 85 (1.18%) | 0 / 79 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0              |
| Dermatitis contact                     |                |                |                |
| subjects affected / exposed            | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)                      | 0              | 0              | 1              |
| Erythema                               |                |                |                |
| subjects affected / exposed            | 0 / 81 (0.00%) | 1 / 85 (1.18%) | 0 / 79 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0              |
| Hyperhidrosis                          |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 85 (1.18%) | 0 / 79 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0              |
| Intertrigo                                      |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 0 / 79 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Pruritus                                        |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 2 / 79 (2.53%) |
| occurrences (all)                               | 0              | 0              | 2              |
| Rash                                            |                |                |                |
| subjects affected / exposed                     | 1 / 81 (1.23%) | 1 / 85 (1.18%) | 0 / 79 (0.00%) |
| occurrences (all)                               | 1              | 1              | 0              |
| Urticaria                                       |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Renal and urinary disorders                     |                |                |                |
| Nephrolithiasis                                 |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 85 (1.18%) | 0 / 79 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0              |
| Renal colic                                     |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Endocrine disorders                             |                |                |                |
| Hypothyroidism                                  |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 85 (1.18%) | 1 / 79 (1.27%) |
| occurrences (all)                               | 0              | 1              | 1              |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Back pain                                       |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Joint swelling                                  |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Muscle spasms                                   |                |                |                |
| subjects affected / exposed                     | 0 / 81 (0.00%) | 1 / 85 (1.18%) | 0 / 79 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0              |
| Osteoarthritis                                  |                |                |                |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)           | 0              | 0              | 1              |
| Pain in extremity           |                |                |                |
| subjects affected / exposed | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 0 / 79 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Rheumatoid arthritis        |                |                |                |
| subjects affected / exposed | 4 / 81 (4.94%) | 2 / 85 (2.35%) | 0 / 79 (0.00%) |
| occurrences (all)           | 6              | 2              | 0              |
| Rheumatoid nodule           |                |                |                |
| subjects affected / exposed | 1 / 81 (1.23%) | 0 / 85 (0.00%) | 0 / 79 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Rotator cuff syndrome       |                |                |                |
| subjects affected / exposed | 0 / 81 (0.00%) | 1 / 85 (1.18%) | 0 / 79 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Sjogren's syndrome          |                |                |                |
| subjects affected / exposed | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 0 / 79 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Spinal osteoarthritis       |                |                |                |
| subjects affected / exposed | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)           | 0              | 0              | 1              |
| Spinal pain                 |                |                |                |
| subjects affected / exposed | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)           | 0              | 0              | 1              |
| Tendonitis                  |                |                |                |
| subjects affected / exposed | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 0 / 79 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Infections and infestations |                |                |                |
| Body tinea                  |                |                |                |
| subjects affected / exposed | 1 / 81 (1.23%) | 0 / 85 (0.00%) | 0 / 79 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Cellulitis                  |                |                |                |
| subjects affected / exposed | 1 / 81 (1.23%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)           | 1              | 0              | 1              |
| Bronchitis                  |                |                |                |
| subjects affected / exposed | 6 / 81 (7.41%) | 1 / 85 (1.18%) | 4 / 79 (5.06%) |
| occurrences (all)           | 6              | 1              | 4              |

|                                     |                |                |                |
|-------------------------------------|----------------|----------------|----------------|
| Cystitis                            |                |                |                |
| subjects affected / exposed         | 0 / 81 (0.00%) | 1 / 85 (1.18%) | 0 / 79 (0.00%) |
| occurrences (all)                   | 0              | 1              | 0              |
| Ear infection                       |                |                |                |
| subjects affected / exposed         | 1 / 81 (1.23%) | 0 / 85 (0.00%) | 0 / 79 (0.00%) |
| occurrences (all)                   | 1              | 0              | 0              |
| Escherichia urinary tract infection |                |                |                |
| subjects affected / exposed         | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 0 / 79 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Fungal skin infection               |                |                |                |
| subjects affected / exposed         | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)                   | 0              | 0              | 1              |
| Gastroenteritis                     |                |                |                |
| subjects affected / exposed         | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 2 / 79 (2.53%) |
| occurrences (all)                   | 0              | 0              | 2              |
| Gastrointestinal viral infection    |                |                |                |
| subjects affected / exposed         | 2 / 81 (2.47%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)                   | 2              | 0              | 1              |
| Gingivitis                          |                |                |                |
| subjects affected / exposed         | 1 / 81 (1.23%) | 0 / 85 (0.00%) | 0 / 79 (0.00%) |
| occurrences (all)                   | 1              | 0              | 0              |
| Herpes simplex                      |                |                |                |
| subjects affected / exposed         | 2 / 81 (2.47%) | 0 / 85 (0.00%) | 0 / 79 (0.00%) |
| occurrences (all)                   | 2              | 0              | 0              |
| Influenza                           |                |                |                |
| subjects affected / exposed         | 0 / 81 (0.00%) | 3 / 85 (3.53%) | 1 / 79 (1.27%) |
| occurrences (all)                   | 0              | 3              | 1              |
| Lyme disease                        |                |                |                |
| subjects affected / exposed         | 1 / 81 (1.23%) | 0 / 85 (0.00%) | 0 / 79 (0.00%) |
| occurrences (all)                   | 1              | 0              | 0              |
| Nasopharyngitis                     |                |                |                |
| subjects affected / exposed         | 6 / 81 (7.41%) | 3 / 85 (3.53%) | 6 / 79 (7.59%) |
| occurrences (all)                   | 6              | 4              | 6              |
| Omphalitis                          |                |                |                |
| subjects affected / exposed         | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)                   | 0              | 0              | 1              |

|                                         |                |                |                |
|-----------------------------------------|----------------|----------------|----------------|
| Periodontitis                           |                |                |                |
| subjects affected / exposed             | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 0 / 79 (0.00%) |
| occurrences (all)                       | 0              | 0              | 0              |
| Pharyngitis                             |                |                |                |
| subjects affected / exposed             | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)                       | 0              | 0              | 1              |
| Pneumonia                               |                |                |                |
| subjects affected / exposed             | 1 / 81 (1.23%) | 0 / 85 (0.00%) | 0 / 79 (0.00%) |
| occurrences (all)                       | 1              | 0              | 0              |
| Respiratory tract infection viral       |                |                |                |
| subjects affected / exposed             | 0 / 81 (0.00%) | 1 / 85 (1.18%) | 1 / 79 (1.27%) |
| occurrences (all)                       | 0              | 1              | 1              |
| Rhinitis                                |                |                |                |
| subjects affected / exposed             | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 2 / 79 (2.53%) |
| occurrences (all)                       | 0              | 0              | 2              |
| Sinusitis                               |                |                |                |
| subjects affected / exposed             | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)                       | 0              | 0              | 1              |
| Skin infection                          |                |                |                |
| subjects affected / exposed             | 1 / 81 (1.23%) | 0 / 85 (0.00%) | 0 / 79 (0.00%) |
| occurrences (all)                       | 1              | 0              | 0              |
| Tinea pedis                             |                |                |                |
| subjects affected / exposed             | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)                       | 0              | 0              | 1              |
| Tinea versicolour                       |                |                |                |
| subjects affected / exposed             | 0 / 81 (0.00%) | 0 / 85 (0.00%) | 1 / 79 (1.27%) |
| occurrences (all)                       | 0              | 0              | 1              |
| Tonsillitis                             |                |                |                |
| subjects affected / exposed             | 1 / 81 (1.23%) | 0 / 85 (0.00%) | 0 / 79 (0.00%) |
| occurrences (all)                       | 1              | 0              | 0              |
| Upper respiratory tract infection       |                |                |                |
| subjects affected / exposed             | 1 / 81 (1.23%) | 1 / 85 (1.18%) | 1 / 79 (1.27%) |
| occurrences (all)                       | 1              | 1              | 1              |
| Viral upper respiratory tract infection |                |                |                |
| subjects affected / exposed             | 0 / 81 (0.00%) | 1 / 85 (1.18%) | 1 / 79 (1.27%) |
| occurrences (all)                       | 0              | 1              | 1              |

|                                                                             |                     |                     |                     |
|-----------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all) | 1 / 81 (1.23%)<br>1 | 1 / 85 (1.18%)<br>1 | 1 / 79 (1.27%)<br>1 |
| Metabolism and nutrition disorders                                          |                     |                     |                     |
| Dyslipidaemia<br>subjects affected / exposed<br>occurrences (all)           | 0 / 81 (0.00%)<br>0 | 1 / 85 (1.18%)<br>1 | 0 / 79 (0.00%)<br>0 |
| Hypercholesterolaemia<br>subjects affected / exposed<br>occurrences (all)   | 1 / 81 (1.23%)<br>1 | 1 / 85 (1.18%)<br>1 | 0 / 79 (0.00%)<br>0 |
| Hyperkalaemia<br>subjects affected / exposed<br>occurrences (all)           | 0 / 81 (0.00%)<br>0 | 0 / 85 (0.00%)<br>0 | 1 / 79 (1.27%)<br>1 |
| Hyperlipidaemia<br>subjects affected / exposed<br>occurrences (all)         | 0 / 81 (0.00%)<br>0 | 0 / 85 (0.00%)<br>0 | 3 / 79 (3.80%)<br>3 |

|                                                                          |                      |  |  |
|--------------------------------------------------------------------------|----------------------|--|--|
| <b>Non-serious adverse events</b>                                        | MAVRILIMUMAB<br>30MG |  |  |
| Total subjects affected by non-serious<br>adverse events                 |                      |  |  |
| subjects affected / exposed                                              | 38 / 81 (46.91%)     |  |  |
| Vascular disorders                                                       |                      |  |  |
| Haematoma<br>subjects affected / exposed<br>occurrences (all)            | 1 / 81 (1.23%)<br>1  |  |  |
| Hot flush<br>subjects affected / exposed<br>occurrences (all)            | 0 / 81 (0.00%)<br>0  |  |  |
| Hypertension<br>subjects affected / exposed<br>occurrences (all)         | 4 / 81 (4.94%)<br>4  |  |  |
| Venous insufficiency<br>subjects affected / exposed<br>occurrences (all) | 0 / 81 (0.00%)<br>0  |  |  |
| General disorders and administration<br>site conditions                  |                      |  |  |
| Fatigue                                                                  |                      |  |  |



|                             |                |  |  |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 81 (1.23%) |  |  |
| occurrences (all)           | 1              |  |  |
| Feeling hot                 |                |  |  |
| subjects affected / exposed | 0 / 81 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Influenza like illness      |                |  |  |
| subjects affected / exposed | 1 / 81 (1.23%) |  |  |
| occurrences (all)           | 1              |  |  |
| Injection site erythema     |                |  |  |
| subjects affected / exposed | 0 / 81 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Injection site haematoma    |                |  |  |
| subjects affected / exposed | 0 / 81 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Injection site swelling     |                |  |  |
| subjects affected / exposed | 1 / 81 (1.23%) |  |  |
| occurrences (all)           | 2              |  |  |
| Injection site reaction     |                |  |  |
| subjects affected / exposed | 0 / 81 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Oedema peripheral           |                |  |  |
| subjects affected / exposed | 1 / 81 (1.23%) |  |  |
| occurrences (all)           | 1              |  |  |
| Pyrexia                     |                |  |  |
| subjects affected / exposed | 1 / 81 (1.23%) |  |  |
| occurrences (all)           | 1              |  |  |
| Immune system disorders     |                |  |  |
| Allergy to arthropod bite   |                |  |  |
| subjects affected / exposed | 0 / 81 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Drug hypersensitivity       |                |  |  |
| subjects affected / exposed | 1 / 81 (1.23%) |  |  |
| occurrences (all)           | 1              |  |  |
| Hypersensitivity            |                |  |  |
| subjects affected / exposed | 1 / 81 (1.23%) |  |  |
| occurrences (all)           | 1              |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| Reproductive system and breast disorders        |                |  |  |
| Cervical dysplasia                              |                |  |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Endometriosis                                   |                |  |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Uterine polyp                                   |                |  |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Vaginal discharge                               |                |  |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Respiratory, thoracic and mediastinal disorders |                |  |  |
| Bronchiectasis                                  |                |  |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Bronchospasm                                    |                |  |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Chronic obstructive pulmonary disease           |                |  |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Cough                                           |                |  |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Obstructive airways disorder                    |                |  |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Oropharyngeal pain                              |                |  |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Pleural effusion                                |                |  |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |

|                                                                                                          |                     |  |  |
|----------------------------------------------------------------------------------------------------------|---------------------|--|--|
| Pulmonary mass<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 81 (0.00%)<br>0 |  |  |
| Rhinorrhoea<br>subjects affected / exposed<br>occurrences (all)                                          | 0 / 81 (0.00%)<br>0 |  |  |
| Psychiatric disorders<br>Anxiety<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 81 (0.00%)<br>0 |  |  |
| Depression<br>subjects affected / exposed<br>occurrences (all)                                           | 2 / 81 (2.47%)<br>2 |  |  |
| Dyssomnia<br>subjects affected / exposed<br>occurrences (all)                                            | 0 / 81 (0.00%)<br>0 |  |  |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 81 (0.00%)<br>0 |  |  |
| Investigations<br>Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all) | 1 / 81 (1.23%)<br>1 |  |  |
| Aspartate aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 81 (1.23%)<br>1 |  |  |
| Blood pressure increased<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 81 (0.00%)<br>0 |  |  |
| Gamma-glutamyltransferase increased<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 81 (1.23%)<br>1 |  |  |
| Weight increased<br>subjects affected / exposed<br>occurrences (all)                                     | 1 / 81 (1.23%)<br>1 |  |  |
| Injury, poisoning and procedural                                                                         |                     |  |  |

|                             |                |  |  |
|-----------------------------|----------------|--|--|
| complications               |                |  |  |
| Alcohol poisoning           |                |  |  |
| subjects affected / exposed | 0 / 81 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Animal bite                 |                |  |  |
| subjects affected / exposed | 1 / 81 (1.23%) |  |  |
| occurrences (all)           | 1              |  |  |
| Bone contusion              |                |  |  |
| subjects affected / exposed | 0 / 81 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Chemical poisoning          |                |  |  |
| subjects affected / exposed | 1 / 81 (1.23%) |  |  |
| occurrences (all)           | 1              |  |  |
| Clavicle fracture           |                |  |  |
| subjects affected / exposed | 0 / 81 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Contusion                   |                |  |  |
| subjects affected / exposed | 0 / 81 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Epicondylitis               |                |  |  |
| subjects affected / exposed | 1 / 81 (1.23%) |  |  |
| occurrences (all)           | 1              |  |  |
| Fall                        |                |  |  |
| subjects affected / exposed | 0 / 81 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Injection related reaction  |                |  |  |
| subjects affected / exposed | 0 / 81 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Laceration                  |                |  |  |
| subjects affected / exposed | 0 / 81 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Limb injury                 |                |  |  |
| subjects affected / exposed | 0 / 81 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Muscle contusion            |                |  |  |

|                                                                                  |                     |  |  |
|----------------------------------------------------------------------------------|---------------------|--|--|
| subjects affected / exposed<br>occurrences (all)                                 | 0 / 81 (0.00%)<br>0 |  |  |
| Cardiac disorders                                                                |                     |  |  |
| Arrhythmia supraventricular<br>subjects affected / exposed<br>occurrences (all)  | 0 / 81 (0.00%)<br>0 |  |  |
| Cardiac failure<br>subjects affected / exposed<br>occurrences (all)              | 0 / 81 (0.00%)<br>0 |  |  |
| Cardiovascular insufficiency<br>subjects affected / exposed<br>occurrences (all) | 0 / 81 (0.00%)<br>0 |  |  |
| Nervous system disorders                                                         |                     |  |  |
| Headache<br>subjects affected / exposed<br>occurrences (all)                     | 5 / 81 (6.17%)<br>5 |  |  |
| Intercostal neuralgia<br>subjects affected / exposed<br>occurrences (all)        | 0 / 81 (0.00%)<br>0 |  |  |
| Sciatica<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 81 (0.00%)<br>0 |  |  |
| Blood and lymphatic system disorders                                             |                     |  |  |
| Anaemia<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 81 (1.23%)<br>1 |  |  |
| Eosinophilia<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 81 (0.00%)<br>0 |  |  |
| Leukocytosis<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 81 (0.00%)<br>0 |  |  |
| Lymphopenia<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 81 (0.00%)<br>0 |  |  |
| Neutropenia                                                                      |                     |  |  |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                            |  |  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|
| subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                                                                                                                                                                                                                                                             | 0 / 81 (0.00%)<br>0                                                                                                                                        |  |  |
| Ear and labyrinth disorders<br>Vertigo<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                                                                                                                                                                                                                   | 1 / 81 (1.23%)<br>1                                                                                                                                        |  |  |
| Eye disorders<br>Conjunctival haemorrhage<br>subjects affected / exposed<br>occurrences (all)<br><br>Conjunctivitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Keratitis<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                                                                 | 0 / 81 (0.00%)<br>0<br><br>0 / 81 (0.00%)<br>0<br><br>0 / 81 (0.00%)<br>0                                                                                  |  |  |
| Gastrointestinal disorders<br>Abdominal pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)<br><br>Cheilitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Constipation<br>subjects affected / exposed<br>occurrences (all)<br><br>Dental caries<br>subjects affected / exposed<br>occurrences (all)<br><br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Dyspepsia | 0 / 81 (0.00%)<br>0<br><br>0 / 81 (0.00%)<br>0<br><br>0 / 81 (0.00%)<br>0<br><br>0 / 81 (0.00%)<br>0<br><br>0 / 81 (0.00%)<br>0<br><br>1 / 81 (1.23%)<br>1 |  |  |

|                                        |                |  |  |
|----------------------------------------|----------------|--|--|
| subjects affected / exposed            | 0 / 81 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Gastritis                              |                |  |  |
| subjects affected / exposed            | 0 / 81 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Gingival swelling                      |                |  |  |
| subjects affected / exposed            | 0 / 81 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Haemorrhoids                           |                |  |  |
| subjects affected / exposed            | 0 / 81 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Irritable bowel syndrome               |                |  |  |
| subjects affected / exposed            | 0 / 81 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Mouth cyst                             |                |  |  |
| subjects affected / exposed            | 0 / 81 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Nausea                                 |                |  |  |
| subjects affected / exposed            | 0 / 81 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Vomiting                               |                |  |  |
| subjects affected / exposed            | 0 / 81 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Hepatobiliary disorders                |                |  |  |
| Hypertransaminasaemia                  |                |  |  |
| subjects affected / exposed            | 0 / 81 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Skin and subcutaneous tissue disorders |                |  |  |
| Dermatitis atopic                      |                |  |  |
| subjects affected / exposed            | 0 / 81 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Dermatitis contact                     |                |  |  |
| subjects affected / exposed            | 0 / 81 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Erythema                               |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Hyperhidrosis                                   |                |  |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Intertrigo                                      |                |  |  |
| subjects affected / exposed                     | 1 / 81 (1.23%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Pruritus                                        |                |  |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Rash                                            |                |  |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Urticaria                                       |                |  |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Renal and urinary disorders                     |                |  |  |
| Nephrolithiasis                                 |                |  |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Renal colic                                     |                |  |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Endocrine disorders                             |                |  |  |
| Hypothyroidism                                  |                |  |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Musculoskeletal and connective tissue disorders |                |  |  |
| Back pain                                       |                |  |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Joint swelling                                  |                |  |  |
| subjects affected / exposed                     | 0 / 81 (0.00%) |  |  |
| occurrences (all)                               | 0              |  |  |
| Muscle spasms                                   |                |  |  |



|                             |                |  |  |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 81 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Osteoarthritis              |                |  |  |
| subjects affected / exposed | 0 / 81 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Pain in extremity           |                |  |  |
| subjects affected / exposed | 1 / 81 (1.23%) |  |  |
| occurrences (all)           | 1              |  |  |
| Rheumatoid arthritis        |                |  |  |
| subjects affected / exposed | 2 / 81 (2.47%) |  |  |
| occurrences (all)           | 3              |  |  |
| Rheumatoid nodule           |                |  |  |
| subjects affected / exposed | 0 / 81 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Rotator cuff syndrome       |                |  |  |
| subjects affected / exposed | 1 / 81 (1.23%) |  |  |
| occurrences (all)           | 1              |  |  |
| Sjogren's syndrome          |                |  |  |
| subjects affected / exposed | 1 / 81 (1.23%) |  |  |
| occurrences (all)           | 1              |  |  |
| Spinal osteoarthritis       |                |  |  |
| subjects affected / exposed | 0 / 81 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Spinal pain                 |                |  |  |
| subjects affected / exposed | 0 / 81 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Tendonitis                  |                |  |  |
| subjects affected / exposed | 1 / 81 (1.23%) |  |  |
| occurrences (all)           | 1              |  |  |
| Infections and infestations |                |  |  |
| Body tinea                  |                |  |  |
| subjects affected / exposed | 0 / 81 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Cellulitis                  |                |  |  |
| subjects affected / exposed | 0 / 81 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |

|                                     |                |  |  |
|-------------------------------------|----------------|--|--|
| Bronchitis                          |                |  |  |
| subjects affected / exposed         | 3 / 81 (3.70%) |  |  |
| occurrences (all)                   | 3              |  |  |
| Cystitis                            |                |  |  |
| subjects affected / exposed         | 1 / 81 (1.23%) |  |  |
| occurrences (all)                   | 1              |  |  |
| Ear infection                       |                |  |  |
| subjects affected / exposed         | 0 / 81 (0.00%) |  |  |
| occurrences (all)                   | 0              |  |  |
| Escherichia urinary tract infection |                |  |  |
| subjects affected / exposed         | 1 / 81 (1.23%) |  |  |
| occurrences (all)                   | 1              |  |  |
| Fungal skin infection               |                |  |  |
| subjects affected / exposed         | 1 / 81 (1.23%) |  |  |
| occurrences (all)                   | 1              |  |  |
| Gastroenteritis                     |                |  |  |
| subjects affected / exposed         | 1 / 81 (1.23%) |  |  |
| occurrences (all)                   | 1              |  |  |
| Gastrointestinal viral infection    |                |  |  |
| subjects affected / exposed         | 0 / 81 (0.00%) |  |  |
| occurrences (all)                   | 0              |  |  |
| Gingivitis                          |                |  |  |
| subjects affected / exposed         | 0 / 81 (0.00%) |  |  |
| occurrences (all)                   | 0              |  |  |
| Herpes simplex                      |                |  |  |
| subjects affected / exposed         | 0 / 81 (0.00%) |  |  |
| occurrences (all)                   | 0              |  |  |
| Influenza                           |                |  |  |
| subjects affected / exposed         | 1 / 81 (1.23%) |  |  |
| occurrences (all)                   | 1              |  |  |
| Lyme disease                        |                |  |  |
| subjects affected / exposed         | 0 / 81 (0.00%) |  |  |
| occurrences (all)                   | 0              |  |  |
| Nasopharyngitis                     |                |  |  |
| subjects affected / exposed         | 4 / 81 (4.94%) |  |  |
| occurrences (all)                   | 5              |  |  |

|                                   |                |  |  |
|-----------------------------------|----------------|--|--|
| Omphalitis                        |                |  |  |
| subjects affected / exposed       | 0 / 81 (0.00%) |  |  |
| occurrences (all)                 | 0              |  |  |
| Periodontitis                     |                |  |  |
| subjects affected / exposed       | 1 / 81 (1.23%) |  |  |
| occurrences (all)                 | 1              |  |  |
| Pharyngitis                       |                |  |  |
| subjects affected / exposed       | 1 / 81 (1.23%) |  |  |
| occurrences (all)                 | 1              |  |  |
| Pneumonia                         |                |  |  |
| subjects affected / exposed       | 0 / 81 (0.00%) |  |  |
| occurrences (all)                 | 0              |  |  |
| Respiratory tract infection viral |                |  |  |
| subjects affected / exposed       | 0 / 81 (0.00%) |  |  |
| occurrences (all)                 | 0              |  |  |
| Rhinitis                          |                |  |  |
| subjects affected / exposed       | 2 / 81 (2.47%) |  |  |
| occurrences (all)                 | 2              |  |  |
| Sinusitis                         |                |  |  |
| subjects affected / exposed       | 0 / 81 (0.00%) |  |  |
| occurrences (all)                 | 0              |  |  |
| Skin infection                    |                |  |  |
| subjects affected / exposed       | 0 / 81 (0.00%) |  |  |
| occurrences (all)                 | 0              |  |  |
| Tinea pedis                       |                |  |  |
| subjects affected / exposed       | 0 / 81 (0.00%) |  |  |
| occurrences (all)                 | 0              |  |  |
| Tinea versicolour                 |                |  |  |
| subjects affected / exposed       | 0 / 81 (0.00%) |  |  |
| occurrences (all)                 | 0              |  |  |
| Tonsillitis                       |                |  |  |
| subjects affected / exposed       | 0 / 81 (0.00%) |  |  |
| occurrences (all)                 | 0              |  |  |
| Upper respiratory tract infection |                |  |  |
| subjects affected / exposed       | 2 / 81 (2.47%) |  |  |
| occurrences (all)                 | 2              |  |  |

|                                                                                             |                     |  |  |
|---------------------------------------------------------------------------------------------|---------------------|--|--|
| Viral upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 2 / 81 (2.47%)<br>2 |  |  |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)                 | 2 / 81 (2.47%)<br>2 |  |  |
| Metabolism and nutrition disorders                                                          |                     |  |  |
| Dyslipidaemia<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 81 (0.00%)<br>0 |  |  |
| Hypercholesterolaemia<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 81 (0.00%)<br>0 |  |  |
| Hyperkalaemia<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 81 (0.00%)<br>0 |  |  |
| Hyperlipidaemia<br>subjects affected / exposed<br>occurrences (all)                         | 2 / 81 (2.47%)<br>2 |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 10 December 2010 | The anticipated number of study centers was increased from 90 to 100. The maximum duration of the study was corrected from 40 weeks to 44 weeks. Reference to the data safety monitoring board (DSMB) was removed from the Study-stopping Criteria section of the protocol. A section describing un-blinding in the event of a suspected unexpected serious adverse reaction (SUSAR) was added to the protocol. Language in the protocol was clarified to state that investigational product was not to be removed from the storage area until all protocol-specific assessments were completed and the subject was ready for dosing. Instructions relating to the preparation of placebo were added to the protocol. In the case of a clinically significant pulmonary abnormality, the language in the protocol was clarified to make it clear that the investigator was the responsible person, in collaboration with the sponsor, to make the decision to resume administration of investigational product. Changes in eligibility criteria. A diffusing capacity for carbon monoxide (DLCO) assessment was added to the protocol. The need for a sample collection for anti-drug antibodies (ADA) analysis in the event of a severe hypersensitivity reaction was removed from the protocol. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Non-compartmental analyses was not performed for pharmacokinetics parameters due to limited sampling schedule

Notes: