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, albulescum@medimmune.com
Scientific contact	Marius Albulescu, Associate Medical Director, MedImmune, LLC, albulescum@medimmune.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	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:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	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
Arm title	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.

Arm title	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.

Arm title	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.

Arm title	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.

Number of subjects in period 1	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

Number of subjects in period 1	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:	
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:	
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:	
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:	
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:	
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:	
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:	
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:	
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:	
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:	
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

Statistical analysis title	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 >=20 percent (%) improvement, in: SJC and TJC and >=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

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)	24.7	50.6	61.2	73.4

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	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

Statistical analysis title	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

Statistical analysis title	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

	(TEAEs)

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 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				
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 (=<) 15%, more than (>) 15 to =<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 =<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 =<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 =<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:

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:

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:

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:

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 >=50% improvement, in: SJC and TJC and >=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

Statistical analysis title	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

Statistical analysis title	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 >=70% improvement, in: SJC and TJC and >=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 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)	3.7	12.3	10.6	13.9

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	= 0.079
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

Statistical analysis title	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

Statistical analysis title	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

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	= 0.009
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

Statistical analysis title	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

Statistical analysis title	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) >=3.2 to less than or equal to (=<) 5.1 or change from baseline >=0.6 to =< 1.2 with baseline DAS28 (CRP) >=3.2 to =<5.1; no response: change from baseline <0.6 or change from baseline >=0.6 and =<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

Statistical analysis title	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

Statistical analysis title	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 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)				
DAS28 (CRP) Remission	4.9	21	17.6	19
Low Disease Activity	8.6	33.3	31.8	41.8

Statistical analyses

Statistical analysis title	Statistical analysis 1

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 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

Statistical analysis title	Statistical analysis 2

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 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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	Statistical analysis 5
Statistical analysis description:	
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

Statistical analysis title	Statistical analysis 6
Statistical analysis description:	
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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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 (± 2.093)	62.65 (± 2.11)	63.58 (± 2.034)	62.35 (± 2.217)
Change at Day 169 (n=40, 65, 73, 74)	-15.2 (± 3.006)	-23.14 (± 2.563)	-23.31 (± 2.446)	-26.53 (± 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

Statistical analysis title	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

Statistical analysis title	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

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	< 0.837
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

Statistical analysis title	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

Statistical analysis title	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

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: cm				
arithmetic mean (standard error)				
Baseline (n=81, 81, 85, 79)	6.6 (± 0.168)	6.6 (± 0.162)	6.81 (± 0.144)	6.42 (± 0.166)
Change at Day 169 (n=40, 65, 73, 74)	-2.39 (± 0.305)	-3.81 (± 0.254)	-3.85 (± 0.241)	-3.95 (± 0.243)

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	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

Statistical analysis title	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

Statistical analysis title	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

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	< 0.479
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

Statistical analysis title	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

Statistical analysis title	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 (± 83.3)	0.8784 (± 102.8)	0.5197 (± 287.4)	0.5856 (± 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

Statistical analysis title	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

Statistical analysis title	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

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	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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:

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.

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	2.4	5.1

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	< 0.21
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

Statistical analysis title	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

Statistical analysis title	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

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	< 0.21
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

Statistical analysis title	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

Statistical analysis title	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 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)	0	3.7	1.2	1.3

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	< 0.245
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

Statistical analysis title	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

Statistical analysis title	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 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 sore 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

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=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

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	< 0.463
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

Statistical analysis title	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

Statistical analysis title	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[1]

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 30 mg	Mavrilimumab 100 mg	Mavrilimumab 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

Statistical analyses

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: -	
Reporting group title	MAVRILIMUMAB 100MG
Reporting group description: -	
Reporting group title	MAVRILIMUMAB 150MG
Reporting group description: -	
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 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 %

Non-serious adverse events	PLACEBO	MAVRILIMUMAB 100MG	MAVRILIMUMAB 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			
subjects affected / exposed	1 / 81 (1.23%)	0 / 85 (0.00%)	0 / 79 (0.00%)
occurrences (all)	1	0	0
Endometriosis			
subjects affected / exposed	0 / 81 (0.00%)	1 / 85 (1.18%)	0 / 79 (0.00%)
occurrences (all)	0	1	0
Uterine polyp			
subjects affected / exposed	0 / 81 (0.00%)	1 / 85 (1.18%)	0 / 79 (0.00%)
occurrences (all)	0	1	0
Vaginal discharge			
subjects affected / exposed	0 / 81 (0.00%)	1 / 85 (1.18%)	0 / 79 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Bronchiectasis			
subjects affected / exposed	0 / 81 (0.00%)	1 / 85 (1.18%)	0 / 79 (0.00%)
occurrences (all)	0	1	0
Bronchospasm			
subjects affected / exposed	1 / 81 (1.23%)	0 / 85 (0.00%)	0 / 79 (0.00%)
occurrences (all)	1	0	0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 81 (0.00%)	1 / 85 (1.18%)	0 / 79 (0.00%)
occurrences (all)	0	1	0
Obstructive airways disorder			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	1 / 79 (1.27%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	1 / 79 (1.27%)
occurrences (all)	0	0	1
Pleural effusion			
subjects affected / exposed	1 / 81 (1.23%)	0 / 85 (0.00%)	0 / 79 (0.00%)
occurrences (all)	1	0	0
Pulmonary mass			

subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	1 / 79 (1.27%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	1 / 81 (1.23%)	0 / 85 (0.00%)	0 / 79 (0.00%)
occurrences (all)	2	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 81 (0.00%)	1 / 85 (1.18%)	0 / 79 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	1 / 79 (1.27%)
occurrences (all)	0	0	1
Dyssomnia			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	1 / 79 (1.27%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	0 / 81 (0.00%)	1 / 85 (1.18%)	0 / 79 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 81 (0.00%)	1 / 85 (1.18%)	1 / 79 (1.27%)
occurrences (all)	0	1	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 81 (0.00%)	1 / 85 (1.18%)	0 / 79 (0.00%)
occurrences (all)	0	1	0
Blood pressure increased			
subjects affected / exposed	1 / 81 (1.23%)	0 / 85 (0.00%)	0 / 79 (0.00%)
occurrences (all)	2	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	0 / 79 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	1 / 81 (1.23%)	1 / 85 (1.18%)	0 / 79 (0.00%)
occurrences (all)	1	1	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			
subjects affected / exposed	0 / 81 (0.00%)	1 / 85 (1.18%)	0 / 79 (0.00%)
occurrences (all)	0	1	0
Cardiac failure			
subjects affected / exposed	1 / 81 (1.23%)	0 / 85 (0.00%)	0 / 79 (0.00%)
occurrences (all)	1	0	0
Cardiovascular insufficiency			
subjects affected / exposed	1 / 81 (1.23%)	0 / 85 (0.00%)	0 / 79 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 81 (2.47%)	4 / 85 (4.71%)	6 / 79 (7.59%)
occurrences (all)	2	4	8
Intercostal neuralgia			
subjects affected / exposed	0 / 81 (0.00%)	1 / 85 (1.18%)	0 / 79 (0.00%)
occurrences (all)	0	1	0
Sciatica			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	1 / 79 (1.27%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 81 (1.23%)	0 / 85 (0.00%)	0 / 79 (0.00%)
occurrences (all)	1	0	0
Eosinophilia			
subjects affected / exposed	0 / 81 (0.00%)	1 / 85 (1.18%)	0 / 79 (0.00%)
occurrences (all)	0	1	0
Leukocytosis			
subjects affected / exposed	2 / 81 (2.47%)	0 / 85 (0.00%)	0 / 79 (0.00%)
occurrences (all)	2	0	0
Lymphopenia			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	1 / 79 (1.27%)
occurrences (all)	0	0	1
Neutropenia			
subjects affected / exposed	1 / 81 (1.23%)	0 / 85 (0.00%)	3 / 79 (3.80%)
occurrences (all)	1	0	4
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	0 / 81 (0.00%)	1 / 85 (1.18%)	0 / 79 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	1 / 79 (1.27%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	0 / 81 (0.00%)	2 / 85 (2.35%)	0 / 79 (0.00%)
occurrences (all)	0	2	0
Keratitis			
subjects affected / exposed	0 / 81 (0.00%)	1 / 85 (1.18%)	0 / 79 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 81 (1.23%)	0 / 85 (0.00%)	1 / 79 (1.27%)
occurrences (all)	1	0	1
Abdominal pain upper			
subjects affected / exposed	1 / 81 (1.23%)	0 / 85 (0.00%)	0 / 79 (0.00%)
occurrences (all)	1	0	0
Cheilitis			
subjects affected / exposed	0 / 81 (0.00%)	1 / 85 (1.18%)	0 / 79 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	1 / 81 (1.23%)	0 / 85 (0.00%)	0 / 79 (0.00%)
occurrences (all)	1	0	0
Dental caries			
subjects affected / exposed	0 / 81 (0.00%)	1 / 85 (1.18%)	1 / 79 (1.27%)
occurrences (all)	0	1	1
Diarrhoea			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	2 / 79 (2.53%)
occurrences (all)	0	0	2
Dyspepsia			
subjects affected / exposed	1 / 81 (1.23%)	1 / 85 (1.18%)	0 / 79 (0.00%)
occurrences (all)	1	1	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			
subjects affected / exposed	1 / 81 (1.23%)	1 / 85 (1.18%)	1 / 79 (1.27%)
occurrences (all)	1	1	1
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	0 / 81 (0.00%)	1 / 85 (1.18%)	0 / 79 (0.00%)
occurrences (all)	0	1	0
Hypercholesterolaemia			
subjects affected / exposed	1 / 81 (1.23%)	1 / 85 (1.18%)	0 / 79 (0.00%)
occurrences (all)	1	1	0
Hyperkalaemia			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	1 / 79 (1.27%)
occurrences (all)	0	0	1
Hyperlipidaemia			
subjects affected / exposed	0 / 81 (0.00%)	0 / 85 (0.00%)	3 / 79 (3.80%)
occurrences (all)	0	0	3

Non-serious adverse events	MAVRILIMUMAB 30MG		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 81 (46.91%)		
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences (all)	1		
Hot flush			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	4 / 81 (4.94%)		
occurrences (all)	4		
Venous insufficiency			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences (all)	0		
General disorders and administration 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			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	2 / 81 (2.47%)		
occurrences (all)	2		
Dyssomnia			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences (all)	0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences (all)	1		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences (all)	1		
Blood pressure increased			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences (all)	0		
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences (all)	1		
Weight increased			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences (all)	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	0 / 81 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Arrhythmia supraventricular			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences (all)	0		
Cardiac failure			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences (all)	0		
Cardiovascular insufficiency			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 81 (6.17%)		
occurrences (all)	5		
Intercostal neuralgia			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences (all)	0		
Sciatica			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 81 (1.23%)		
occurrences (all)	1		
Eosinophilia			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences (all)	0		
Leukocytosis			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences (all)	0		
Lymphopenia			
subjects affected / exposed	0 / 81 (0.00%)		
occurrences (all)	0		
Neutropenia			

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

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

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 subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 2 / 81 (2.47%) 2 2 / 81 (2.47%) 2		
Metabolism and nutrition disorders Dyslipidaemia subjects affected / exposed occurrences (all) Hypercholesterolaemia subjects affected / exposed occurrences (all) Hyperkalaemia subjects affected / exposed occurrences (all) Hyperlipidaemia subjects affected / exposed occurrences (all)	 0 / 81 (0.00%) 0 0 / 81 (0.00%) 0 0 / 81 (0.00%) 0 2 / 81 (2.47%) 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:

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: