Clinical trial results:
A Phase 2 Exploratory Study of Mavrilimumab versus Anti-tumor Necrosis Factor in Subjects with Rheumatoid Arthritis

Summary

EudraCT number	2011-005649-10
Trial protocol	DE ES PT GR HU CZ SK GB
Global end of trial date	06 February 2015

Results information

Result version number	v2 (current)
This version publication date	13 November 2016
First version publication date	16 March 2016
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	CD-IA-CAM-3001-1107

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01715896
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, +44 301-398-0000, albulescum@medimmune.com
Scientific contact	Marius Albulescu, Associate Medical Director, MedImmune, LLC, +44 301-398-0000, 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	06 February 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 February 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to explore the efficacy of mavrilimumab compared with golimumab in the treatment of adult participants 18-80 years of age with moderate-to-severe active rheumatoid arthritis (RA) who had an inadequate response to one or more conventional disease-modifying anti-rheumatic drugs (DMARDs) and/or one or two anti-tumor necrosis factor (TNF) agents (excluding golimumab) for efficacy or safety reasons.

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:

Participants with inadequate response to one or more conventional DMARDs and/or participants previously treated with one or two anti-TNF agents other than golimumab given for at least 3 months at various doses where the last agent was discontinued within 2 years prior to Day 1 due to inadequate response, safety, or intolerance, with the exception of the occurrence of serious adverse events (SAEs). Recommended Dose Regimens of Previous Anti-TNF Treatment were Adalimumab (Dosage of atleast 40 milligram [mg] every other week subcutaneous route), Infliximab (Dosage of at least 3 milligram per kilogram [mg/kg] at Weeks 0, 2, and 6, followed by a maintenance dose every 8 weeks thereafter intravenous route), Etanercept (Dosage of at least 25 mg administered twice weekly or 50 mg once weekly subcutaneous route) and Certolizumab (Dosage of 400 mg at Weeks 0, 2, and 4, followed by a maintenance dose of 200 mg every 2 weeks subcutaneous route). 'The last dose of anti-TNF agent should have been given at least 8 weeks prior to Day 1.

Evidence for comparator: -

Actual start date of recruitment	19 March 2013
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: 21
Country: Number of subjects enrolled	Colombia: 10
Country: Number of subjects enrolled	Czech Republic: 26
Country: Number of subjects enrolled	Greece: 5
Country: Number of subjects enrolled	Hungary: 5
Country: Number of subjects enrolled	Israel: 12

Country: Number of subjects enrolled	Mexico: 12
Country: Number of subjects enrolled	Portugal: 2
Country: Number of subjects enrolled	Russian Federation: 22
Country: Number of subjects enrolled	Serbia: 5
Country: Number of subjects enrolled	Slovakia: 1
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	United Kingdom: 11
Worldwide total number of subjects	138
EEA total number of subjects	56

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)	118
From 65 to 84 years	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Overall, 215 participants were screened, of which 77 participants were considered as screen failures and 138 participants were randomized and completed 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	Golimumab 50 mg alternating with Placebo

Arm description:

Participants received alternating doses of golimumab 50 mg (Weeks 0, 4, 8, 12, 16, 20, and 24) and placebo matched to mavrilimumab (Weeks 2, 6, 10, 14, 18, and 22) injections 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	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 (Weeks 2, 6, 10, 14, 18, and 22) injections subcutaneously in combination with stable dose of methotrexate (7.5 to 25 mg per week) through oral or parenteral route.

Investigational medicinal product name	Golimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received golimumab 50 mg (Weeks 0, 4, 8, 12, 16, 20, and 24) injections subcutaneously 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:

Participants received mavrilimumab 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
Investigational medicinal product code	CAM-3001
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received mavrilimumab 100 mg injection subcutaneously every 2 weeks for 24 weeks.

Number of subjects in period 1	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg
Started	68	70
Completed	65	59
Not completed	3	11
Consent withdrawn by subject	1	4
Unspecified	2	5
Lost to follow-up	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Golimumab 50 mg alternating with Placebo
Reporting group description:	
Participants received alternating doses of golimumab 50 mg (Weeks 0, 4, 8, 12, 16, 20, and 24) and placebo matched to mavrilimumab (Weeks 2, 6, 10, 14, 18, and 22) injections 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:	
Participants received mavrilimumab 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 values	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg	Total
Number of subjects	68	70	138
Age categorical Units: Subjects			
Adults (18-64 years)	59	59	118
Elderly (From 65-84 years)	9	11	20
Age Continuous | Units: years			
arithmetic mean	49.9	50.2	
standard deviation	± 11.4	± 13.3	-
Gender, Male/Female Units: Participants			
Female	57	56	113
Male	11	14	25

End points

End points reporting groups

Reporting group title	Golimumab 50 mg alternating with Placebo

Reporting group description:

Participants received alternating doses of golimumab 50 mg (Weeks 0, 4, 8, 12, 16, 20, and 24) and placebo matched to mavrilimumab (Weeks 2, 6, 10, 14, 18, and 22) injections 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:

Participants received mavrilimumab 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.

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:

The ACR20 was defined as greater than or equal to (>=) 20 percent (%) improvement, in: swollen joint count (SJC) and tender joint count (TJC) and >=20% improvement in at least 3 of 5 remaining ACR core measures: participant assessment of pain; participant global assessment of disease activity (PGA); physician global assessment of disease activity (MDGA); self-assessed disability (disability index of the Health Assessment Questionnaire [HAQ]); and C-reactive protein (CRP). If CRP was missing and Erythrocyte sedimentation rate (ESR) was present then ESR was to be used. The mITT population analysis set included all participants in the treatment group corresponding to their randomized treatment group. The percentage of participants were calculated by logistic regression model method.

End point type	Primary

End point timeframe:

Day 169

End point values	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	70		
Units: percentage of participants				
number (not applicable)	65.6	62		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis reported for Percentage of Participants who Achieved ACR20 Responses at Day 169. P-value and 90% unconditional exact confidence interval (CI) was calculated using the model of logit (response) = strata + treatment.

Comparison groups	Mavrilimumab 100 mg v Golimumab 50 mg alternating with Placebo

Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.666
Method	Logit response Model
Parameter estimate	Percent difference
Point estimate	-3.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-16.8
upper limit	9.8

Primary: 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:

The 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. If CRP was missing and ESR was present then ESR was to be used. The mITT population analysis set included all participants in the treatment group corresponding to their randomized treatment group. The percentage of participants were calculated by logistic regression model method.

End point type	Primary

End point timeframe:

Day 169

End point values	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	70		
Units: percentage of participants				
number (not applicable)	43.4	34.8		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis reported for percentage of Participants who Achieved ACR50 Responses at Day 169. P-value and 90% unconditional exact CI was calculated using the model of logit (response) = strata + treatment.

Comparison groups	Mavrilimumab 100 mg v Golimumab 50 mg alternating with Placebo

Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.293
Method	Logit response Model
Parameter estimate	Percent difference
Point estimate	-8.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	-22
upper limit	4.8

Primary: 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:

The 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. If CRP was missing and ESR was present then ESR was to be used. The mITT population analysis set included all participants in the treatment group corresponding to their randomized treatment group. The percentage of participants were calculated by logistic regression model method.

End point type	Primary

End point timeframe:

Day 169

End point values	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	70		
Units: percentage of participants				
number (not applicable)	25.9	16.1		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis reported for percentage of Participants who Achieved ACR70 Responses at Day 169. P-value and 90% unconditional exact CI was calculated using the model of logit (response) = strata + treatment.

Comparison groups	Mavrilimumab 100 mg v Golimumab 50 mg alternating with Placebo

Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.156
Method	Logit Response Model
Parameter estimate	Percent difference
Point estimate	-9.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-21.1
upper limit	1.4

Primary: Percentage of Participants who Achieved Disease Activity Score of 28 Joints Using C-Reactive Protein (DAS28 [CRP]) Response at Day 169

End point title	Percentage of Participants who Achieved Disease Activity Score of 28 Joints Using C-Reactive Protein (DAS28 [CRP]) Response at Day 169

End point description:

The DAS28 (CRP) was calculated from the number of SJC and TJC using the 28 joints count, The DAS28(CRP) considers 28 of the 68 TJC and 28 of the 66 SJC and participant's global health (GH) using PGA of disease activity using the visual analogue scale (VAS) of 0 (= best), 100 (= worst) plus levels of CRP (milligram/Liter [mg/L]). Total score range: 0-9.4, higher score= more disease activity. DAS28 (CRP) less than (<) 3.2 = low disease activity, >=3.2 to 5.1 = moderate to high disease activity and <2.6= remission. Participants with score less than 2.6 were analysed. The mITT population analysis set included all participants in the treatment group corresponding to their randomized treatment group. The percentage of participants were calculated by logistic regression model method.

End point type	Primary

End point timeframe:

Day 169

End point values	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	70		
Units: percentage of participants				
number (not applicable)	29	17.4		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis reported for Percentage of Participants who Achieved Disease Activity Score of 28 Joints Using C-Reactive Protein (DAS28 [CRP]) Response at Day 169. P-value and 90% unconditional exact CI was calculated using the model of logit (response) = strata + treatment.

Comparison groups	Mavrilimumab 100 mg v Golimumab 50 mg alternating with Placebo

Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.108
Method	Logit Response Model
Parameter estimate	Percent difference
Point estimate	-11.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	-23.2
upper limit	0

Primary: Percentage of Participants who Achieved Health Assessment Questionnaire Disability Index (HAQ-DI) Score Improvement From Baseline and >= 0.25 at Day 169

End point title	Percentage of Participants who Achieved Health Assessment Questionnaire Disability Index (HAQ-DI) Score Improvement From Baseline and >= 0.25 at Day 169

End point description:

The HAQ-DI: 20-item scale assessing participant-reported assessment of ability to perform tasks in 8 categories of daily living activities: dress/groom; arising, eating, hygiene, walking, reaching, grip, and errands/chores 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. Participants with change from baseline more than or equal to (>=) 0.25 were reported. The mITT population analysis set included all participants in the treatment group corresponding to their randomized treatment group. The percentage of participants were calculated by logistic regression model method.

End point type	Primary

End point timeframe:

Day 169

End point values	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	70		
Units: percentage of participants				
number (not applicable)	69	58.7		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis reported for Percentage of Participants who Achieved Health Assessment Questionnaire Disability Index (HAQ-DI) Score >= 0.25 at Day 169. P-value and 90% unconditional exact CI was calculated using the model of logit (response) = strata + treatment.

Comparison groups	Mavrilimumab 100 mg v Golimumab 50 mg alternating with Placebo
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.208
Method	Logit Response Model
Parameter estimate	Percent difference
Point estimate	-10.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-23.7
upper limit	3

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

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

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. TEAE and TESAE were reported as per relatedness and severity. The safety population included all participants who received any amount of study medication.

End point type	Secondary

End point timeframe:

Baseline up to Day 169

End point values	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	70		
Units: participants				
TEAEs	29	36		
TESAEs	3	2		
Investigational-product-related TEAE	12	11		
Severe TEAE	1	3		
Acute TEAEs	5	7		
Acute Severe TEAE	0	1		
Investigational-product-related TESAE	0	2		

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 (leukocytosis, neutropenia, anaemia of chronic disease); serum chemistry (alanine aminotransferase, blood parathyroid hormone, gamma glutamyl transferase, hepatic enzyme, dyslipidaemia, hypercholesterolaemia, hyperglycaemia, hyperlipidaemia, hypertriglyceridaemia); urinalysis. The safety population included all participants who received any amount of study medication.

End point type	Secondary

End point timeframe:

Baseline up to Day 169

End point values	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	70		
Units: participants				
Leukocytosis	0	2		
Neutropenia	0	0		
Anaemia of chronic disease	0	0		
Alanine aminotransferase increased	2	0		
Blood parathyroid hormone increased	0	1		
Gamma-glutamyltransferase increased	1	0		
Hepatic enzyme increased	2	3		
Dyslipidaemia	2	0		
Hypercholesterolaemia	2	0		
Hyperglycaemia	0	1		
Hyperlipidaemia	0	1		
Hypertriglyceridaemia	0	1		
Urinalysis	0	0		

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 amount of study medication.

End point type	Secondary

End point timeframe:

Baseline up to Day 169

End point values	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	70		
Units: participants				
Hypertension	0	1		
Pyrexia	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Pulmonary Function Test Values Below Threshold Values Based on Percent Change From Baseline at Day 85 and 169

End point title	Number of Participants With Pulmonary Function Test Values Below Threshold Values Based on Percent Change From Baseline at Day 85 and 169

End point description:

Pulmonary function testing were performed by spirometry to assess forced expiratory volume in 1 second (FEV1), in 6 second (FEV6), forced vital capacity (FVC), and diffusing capacity for carbon monoxide (DLCO). FEV1 was maximal volume of air exhaled in first second of a forced expiration from a position of full inspiration. FVC was the volume of air which can be forcibly exhaled from the lungs after taking the deepest breath possible. DLCO is a pulmonary function test that measures the partial pressure difference between inspired and expired carbon monoxide. The percentage of predicted values of these pulmonary function tests were calculated based on decreases from baseline and categorized as more than (>) 20% reduction (RD) and absolute value (AV) less than (<) 80% predicted (PR). The safety population included all participants who received any amount of investigational product.

End point type	Secondary

End point timeframe:

Day 85 and 169

End point values	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68[1]	70[2]		
Units: participants				
Day 85: FEV1 >20% RD (n=64, 63)	1	0		
Day 169: FEV1 >20% RD (n=64, 64)	4	1		
Day 85: FEV1 >20% RD and AV <80% PR (n=64, 63)	1	0		

Day 169: FEV1 >20% RD and AV <80% PR (n=64, 64)	4	1		
Day 85: FEV6 >20% RD (n=54, 55)	1	1		
Day 169: FEV6 >20% RD (n=54, 56)	4	0		
Day 85: FEV6 >20% RD and AV <80% PR (n=54, 55)	0	1		
Day 169: FEV6 >20% RD and AV <80% PR (n=54, 56)	2	0		
Day 85: FVC >20% RD (n=64, 63)	0	0		
Day 169: FVC >20% RD (n=64, 64)	2	1		
Day 85: FVC >20% RD and AV <80% PR (n=64, 63)	0	0		
Day 169: FVC >20% RD and AV <80% PR (n=64, 64)	2	1		
Day 85: DLCO >15-20% RD (n=18, 21)	1	0		
Day 169: DLCO >15-20% RD (n=22, 23)	0	0		
Day 85: DLCO >20% RD (n=18, 21)	1	0		
Day 169: DLCO >20% RD (n=22, 23)	1	0		

Notes:

[1] - "n" signifies participants evaluable for the specified value parameter for each arm, respectively.

[2] - "n" signifies participants evaluable for the specified value parameter for each arm, respectively.

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 was 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 indicated greater difficulty in breathing. The safety population included all participants who received any amount 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	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	63		
Units: units on a scale				
arithmetic mean (standard deviation)	0.34 (± 0.81)	0.42 (± 0.73)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Disease Activity Score of 28 Joints Using C-Reactive Protein (DAS28 [CRP]) Score at Day 169

End point title	Change From Baseline in Disease Activity Score of 28 Joints Using C-Reactive Protein (DAS28 [CRP]) Score at Day 169

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. 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 threshold value mentioned parameter for each arm, respectively.

End point type	Secondary

End point timeframe:

Baseline and Day 169

End point values	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	70		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline (n=68, 70)	5.72 (± 0.83)	5.82 (± 0.96)		
Day 169 (n=62, 62)	-2.4 (± 1.42)	-2.11 (± 1.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Continuous American College of Rheumatology (ACRn) Score at Day 169

End point title	Change From Baseline in Continuous 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. Mean indicates adjusted mean (Adj mean). 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 up to Day 169

End point values	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	61		
Units: units on a scale				
arithmetic mean (standard error)	40.49 (± 5.406)	33.06 (± 5.199)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis reported for Change From Baseline in Continuous American College of Rheumatology (ACRn) Score at Day 169. An estimate of the treatment difference and its 90% CI was computed by means of repeated measures model, adjusted for baseline and including a treatment by visit interaction term.

Comparison groups	Mavrilimumab 100 mg v Golimumab 50 mg alternating with Placebo
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.213
Method	Repeated measures model
Parameter estimate	Adjusted Mean difference
Point estimate	-7.42
Confidence interval	
level	90 %
sides	2-sided
lower limit	-17.24
upper limit	2.4

Secondary: American College of Rheumatology (ACR) Hybrid Score at Day 169

End point title	American College of Rheumatology (ACR) Hybrid Score at Day 169

End point description:

ACR Hybrid score 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	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	70		
Units: units on a scale				
median (full range (min-max))	49.99 (-9 to 98.2)	41.66 (-1 to 90.3)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number 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	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	70		
Units: participants				
No response	12	16		
Moderate response	28	35		
Good response	28	19		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis reported for Number of Participants who Achieved DAS28 (CRP) Response by European League Against Rheumatism (EULAR) Category at Day 169. Odds ratio, 90% CI and p-value were was calculated using proportional odds analysis of response model including treatment as a factor.

Comparison groups	Mavrilimumab 100 mg v Golimumab 50 mg alternating with

	Placebo
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.129
Method	Proportional odds analysis
Parameter estimate	Odds ratio (OR)
Point estimate	0.61
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.36
upper limit	1.04

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

End point title	Number 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	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	70		
Units: participants				
DAS28 (CRP) Remission	20	12		
Low Disease Activity	28	20		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis reported for Number of Participants With DAS28 (CRP) Remission at Day 169. 90% CI was calculated for the treatment difference in proportion of responders using logisitic regression with strata and treatment as factors.

Comparison groups	Mavrilimumab 100 mg v Golimumab 50 mg alternating with Placebo

Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.108 [3]
Method	Regression, Logistic
Parameter estimate	Percent difference
Point estimate	-11.6
Confidence interval	
level	90 %
sides	2-sided
lower limit	-23.2
upper limit	0

Notes:

[3] - P-value estimated from fisher's exact test when number of golimumab or active responders was less than 5.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Analysis reported for Number of Participants With Low Disease Activity at Day 169. 90% CI was calculated for the treatment difference in proportion of responders using logisitic regression with strata and treatment as factors.

Comparison groups	Mavrilimumab 100 mg v Golimumab 50 mg alternating with Placebo
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.145
Method	Regression, Logistic
Parameter estimate	Percent difference
Point estimate	-11.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-24.8
upper limit	1.4

Secondary: Time to Onset DAS28 (CRP) remission at Day 169

End point title	Time to Onset DAS28 (CRP) remission at Day 169

End point description:

The DAS28 (CRP) was calculated from the number of SJC and TJC using the 28 joints count, The DAS28 (CRP) considers 28 of the 68 TJC and 28 of the 66 SJC and participant's global health (GH) using PGA of disease activity using the VAS of 0 (= best), 100 (= worst) plus levels of CRP (mg/L). Total score range: 0-9.4, higher score= more disease activity. DAS28 (CRP) <3.2 = low disease activity, >=3.2 to 5.1 = moderate to high disease activity and <2.6= remission. Participants with score less than 2.6 were analysed. Onset of DAS28(CRP) remission <=2.6 defined as the first study day in which the DAS28 score met the criteria. The mITT population analysis set included all participants who were at risk in the treatment group corresponding to their randomized treatment group. Here, "N" is number of participants analysed for this outcome measure.

End point type	Secondary

End point timeframe:

Day 169

End point values	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	12		
Units: days				
median (confidence interval 90%)	57 (29 to 112)	113 (57 to 141)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Golimumab 50 mg alternating with Placebo v Mavrilimumab 100 mg
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.328 [4]
Method	Logrank

Notes:

[4] - P-value was calculated using the Log rank test

Secondary: Duration of DAS28 (CRP) Remission at Day 169

End point title	Duration of DAS28 (CRP) Remission at Day 169

End point description:

The DAS28 (CRP) was calculated from the number of SJC and TJC using the 28 joints count, The DAS28(CRP) considers 28 of the 68 TJC and 28 of the 66 SJC and participant's global health (GH) using PGA of disease activity using the VAS of 0 (= best), 100 (= worst) plus levels of CRP (mg/L). Total score range: 0-9.4, higher score= more disease activity. DAS28 (CRP) <3.2 = low disease activity, >=3.2 to 5.1 = moderate to high disease activity and <2.6= remission. Participants with score less than 2.6 were analysed. Duration of DAS28(CRP) remission for each subject was defined as number of days from onset of remission to when the subject was no longer in remission. The mITT population analysis set included all participants who were at risk in the treatment group corresponding to their randomized treatment group. Here, "N" is number of participants analysed for this outcome measure.

End point type	Secondary

End point timeframe:

Day 169

End point values	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	12		
Units: days				
arithmetic mean (standard error)	105 (± 0.24)	69.6 (± 0.15)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Mavrilimumab 100 mg v Golimumab 50 mg alternating with Placebo
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.003 [5]
Method	Weibull model

Notes:

[5] - P-value was calculated using an Weibull model.

Secondary: Percentage of Participants who Achieved Disease Activity Score of 28 Joints Using Erythrocyte Sedimentation Rate (DAS28 [ESR]) < 2.6 at Day 169

End point title	Percentage of Participants who Achieved Disease Activity Score of 28 Joints Using Erythrocyte Sedimentation Rate (DAS28 [ESR]) < 2.6 at Day 169

End point description:

The DAS28 (ESR) calculated SJC and TJC using the 28 joints, GH using participant assessment of disease activity (participant rated arthritis activity using the numerical rating scale with 0 = best, 10 = worst), and the erythrocyte sedimentation rate (ESR) (millimeters per hour [mm/hour]). Total score range: 0-9.4, higher score = more disease activity. DAS28 (ESR) <3.2 = low disease activity, >=3.2 to 5.1 = moderate to high disease activity and <2.6= remission. The mITT population analysis set included all participants in the treatment group corresponding to their randomized treatment group. The percentage of participants were calculated by logistic regression model method.

End point type	Secondary

End point timeframe:

Day 169

End point values	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	70		
Units: percentage of participants				
number (not applicable)	19	17.3		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis reported for Percentage of Participants who Achieved Disease Activity Score of 28 Joints Using

Erythrocyte Sedimentation Rate (DAS28 [ESR]) at Day 169. 90% CI was calculated for the treatment difference in proportion of responders using logisitic regression with strata and treatment as factors.

Comparison groups	Mavrilimumab 100 mg v Golimumab 50 mg alternating with Placebo
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.795 [6]
Method	Regression, Logistic
Parameter estimate	Percent difference
Point estimate	-1.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-12.4
upper limit	9

Notes:

[6] - P-value estimated from fisher's exact test when number of golimumab or active responders was less than 5.

Secondary: Percentage of Participants who Achieved Simplified Disease Activity Index (SDAI) remission at Day 169

End point title	Percentage of Participants who Achieved 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 centimetre (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. The percentage of participants were calculated by logistic regression model method.

End point type	Secondary

End point timeframe:

Day 169

End point values	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	70		
Units: percentage of participants				
number (not applicable)	18.9	7.2		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis reported for Percentage of Participants who Achieved Simplified Disease Activity Index (SDAI) remission at Day 169. 90% CI was calculated for the treatment difference in proportion of responders using logisitic regression with strata and treatment as factors.

Comparison groups	Mavrilimumab 100 mg v Golimumab 50 mg alternating with Placebo
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.048
Method	Regression, Logistic
Parameter estimate	Percent difference
Point estimate	-11.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-21
upper limit	-2.5

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	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	70		
Units: percentage of participants				
number (not applicable)	17.6	5.7		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis reported for Percentage of Participants With Clinical Disease Activity Index (CDAI) Remission at Day 169. 90% CI was calculated for the treatment difference in proportion of responders using logisitic regression with strata and treatment as factors.

Comparison groups	Mavrilimumab 100 mg v Golimumab 50 mg alternating with Placebo

Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.035
Method	Regression, Logistic
Parameter estimate	Percent difference
Point estimate	-11.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-20.6
upper limit	-3.1

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:

The 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	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	70		
Units: percentage of participants				
number (not applicable)	8.9	1.4		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis reported for Percentage of Participants With American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) Remission at Day 169. 90% CI was calculated for the treatment difference in proportion of responders using logisitic regression with strata and treatment as factors.

Comparison groups	Mavrilimumab 100 mg v Golimumab 50 mg alternating with Placebo

Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.061
Method	Regression, Logistic
Parameter estimate	Percent difference
Point estimate	-7.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-13.6
upper limit	-1.5

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. Mean here indicates adjusted mean. 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	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	70		
Units: joint count				
arithmetic mean (standard error)				
SJC: Baseline (n=68, 70)	14.49 (± 0.779)	14.07 (± 0.824)		
SJC: Change at Day 169 (n=64, 64)	-10.07 (± 0.777)	-10.08 (± 0.747)		
TJC: Baseline (n=68, 70)	24.93 (± 1.662)	25.04 (± 1.543)		
TJC: Change at Day 169 (n=64, 64)	-15.42 (± 1.457)	-14.19 (± 1.399)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis reported for change from baseline in swollen joint count at Day 169. An estimate of the treatment difference and its 90% CI was computed by means of repeated measures model, adjusted for baseline and including terms for treatment group, visit and treatment by visit interaction.

Comparison groups	Mavrilimumab 100 mg v Golimumab 50 mg alternating with Placebo
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.993
Method	Repeated measures model
Parameter estimate	Adjusted mean difference
Point estimate	-0.01
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.33
upper limit	1.32

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Analysis reported for change from baseline in Tender joint count at Day 169. An estimate of the treatment difference and its 90% CI was computed by means of repeated measures model, adjusted for baseline and including terms for treatment group, visit and treatment by visit interaction.

Comparison groups	Mavrilimumab 100 mg v Golimumab 50 mg alternating with Placebo
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.424
Method	Repeated measures model
Parameter estimate	Adjusted mean difference
Point estimate	1.23
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.31
upper limit	3.77

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	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	70		
Units: millimeter (mm)				
arithmetic mean (standard error)				
Baseline (n=68, 70)	66.93 (± 2.352)	69.81 (± 2.015)		
Change at Day 169 (n=64, 64)	-29.61 (± 3.843)	-24.72 (± 3.727)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis reported for Mean Change From Baseline in Patient Assessment of Pain at Day 169. An estimate of the treatment difference and its 90% CI was computed by means of repeated measures model, adjusted for baseline and including terms for treatment group, visit and treatment by visit interaction.

Comparison groups	Mavrilimumab 100 mg v Golimumab 50 mg alternating with Placebo
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.272
Method	Repeated measures model
Parameter estimate	Adjusted mean difference
Point estimate	4.89
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.46
upper limit	12.24

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 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	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	70		
Units: mm				
arithmetic mean (standard error)				
Baseline (n=68, 70)	67.57 (± 2.219)	68.53 (± 2.212)		
Change at Day 169 (n=64, 64)	-28.5 (± 3.773)	-24.04 (± 3.671)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: Analysis reported for Mean Change From Baseline in Patient Global Assessment (PGA) of Disease Activity at Day 169. An estimate of the treatment difference and its 90% CI was computed by means of repeated measures model, adjusted for baseline and including terms for treatment group, visit and treatment by visit interaction.	
Comparison groups	Mavrilimumab 100 mg v Golimumab 50 mg alternating with Placebo
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.319
Method	Repeated measures model
Parameter estimate	Adjusted mean difference
Point estimate	4.46
Confidence interval	
level	90 %
sides	2-sided
lower limit	-2.92
upper limit	11.84

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 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	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	70		
Units: centimeter (cm)				
arithmetic mean (standard error)				
Baseline (n=68, 70)	6.89 (± 0.159)	7.04 (± 0.169)		
Change at Day 169 (n=64, 64)	-4.28 (± 0.317)	-4.11 (± 0.307)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis reported for Mean Change From Baseline in Physician Global Assessment of Disease Activity (MDGA) at Day 169. An estimate of the treatment difference and its 90% CI was computed by means of repeated measures model, adjusted for baseline and including terms for treatment group, visit and treatment by visit interaction.

Comparison groups	Mavrilimumab 100 mg v Golimumab 50 mg alternating with Placebo
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.64
Method	Repeated measures model
Parameter estimate	Adjusted mean difference
Point estimate	0.16
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.42
upper limit	0.74

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	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	70		
Units: units on a scale				
arithmetic mean (standard error)				
Baseline (n=68, 70)	1.58 (± 0.063)	1.59 (± 0.07)		
Change at Day 169 (n=64, 64)	-0.59 (± 0.081)	-0.4 (± 0.078)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis reported for Mean Change from Baseline in Health Assessment Questionnaire Disability Index (HAQ-DI) Score at Day 169. An estimate of the treatment difference and its 90% CI was computed by means of repeated measures model, adjusted for baseline and including terms for treatment group, visit and treatment by visit interaction.

Comparison groups	Mavrilimumab 100 mg v Golimumab 50 mg alternating with Placebo
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.055
Method	Repeated measures model
Parameter estimate	Adjusted mean difference
Point estimate	0.18
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.03
upper limit	0.34

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

End point title	Ratio of Change C-Reactive Protein (CRP) at Day 169 to Baseline

End point description:

The ratio of change from baseline for CRP was analyzed and reported. The 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 and Day 169

End point values	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	64		
Units: ratio				
geometric mean (geometric coefficient of variation)	0.5036 (± 344)	0.5142 (± 100.9)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis reported for Ratio of Change C-Reactive Protein (CRP) at Day 169 to Baseline. An estimate of the treatment difference and its 90% CI was computed by means of repeated measures model including terms for baseline as a continuous covariate and treatment as a factor was used for the analysis.

Comparison groups	Mavrilimumab 100 mg v Golimumab 50 mg alternating with Placebo
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.752
Method	Repeated measures model
Parameter estimate	Adjusted geometric mean ratio
Point estimate	1.06
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.79
upper limit	1.41

Secondary: Erythrocyte Sedimentation Rate (ESR) at Day 169

End point title	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. "n'' signifies participants evaluable for specified category for each arm, respectively.

End point type	Secondary

End point timeframe:

Day 169

End point values	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	64		
Units: millimeter per hour (mm/h)				
geometric mean (standard deviation)	26.8 (± 21)	27.8 (± 20.8)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Analysis reported for Ratio of Erythrocyte Sedimentation Rate (ESR) at Day 169 to Baseline. An estimate of the treatment difference and its 90% CI was computed by means of repeated measures model including terms for baseline as a continuous covariate and treatment as a factor was used for the analysis.

Comparison groups	Mavrilimumab 100 mg v Golimumab 50 mg alternating with Placebo
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.725
Method	Repeated measures model
Parameter estimate	Adjusted geometric mean ratio
Point estimate	1.05
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.84
upper limit	1.3

Secondary: Serum Concentrations of Mavrilimumab

End point title	Serum Concentrations of Mavrilimumab[7]

End point description:

Serum concentrations after subcutaneous dose of mavrilimumab were calculated. 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 this arm respectively.

End point type	Secondary

End point timeframe:

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

Notes:

[7] - 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: This end-point was related to only serum concentrations after subcutaneous dose of mavrilimumab and hence, not reporting statistics for all the arms in the baseline period.

End point values	Mavrilimumab 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	70			
Units: nanogram per milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)				
Baseline (n=69)	0 (± 512.9)			
Day 8 (n=66)	2837.24 (± 49.1)			
Day 15 (n=67)	1084.43 (± 143.6)			
Day 29 (n=69)	2094.7 (± 58.9)			
Day 85 (n=67)	2886.71 (± 64.1)			
Day 141 (n=63)	1731.65 (± 79.3)			
Day 169 (n=64)	1701.13 (± 67.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Exhibiting Anti-Drug Antibodies (ADAs) to Mavrilimumab

End point title	Number of Participants Exhibiting Anti-Drug Antibodies (ADAs) to Mavrilimumab

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	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	70		
Units: participants				
number (not applicable)	3	3		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Day 169

Adverse event reporting additional description:

The safety population included all participants who received any amount of study medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Golimumab 50 mg alternating with Placebo

Reporting group description:

Participants received alternating doses of golimumab 50 mg (Weeks 0, 4, 8, 12, 16, 20, and 24) and placebo matched to mavrilimumab (Weeks 2, 6, 10, 14, 18, and 22) injections 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:

Participants received mavrilimumab 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.

Serious adverse events	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 68 (4.41%)	2 / 70 (2.86%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	1 / 68 (1.47%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Parathyroid tumour benign			
subjects affected / exposed	0 / 68 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Vertebrobasilar insufficiency			

subjects affected / exposed	0 / 68 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastroduodenitis			
subjects affected / exposed	1 / 68 (1.47%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer			
subjects affected / exposed	1 / 68 (1.47%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Lung disorder			
subjects affected / exposed	1 / 68 (1.47%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 68 (1.47%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Golimumab 50 mg alternating with Placebo	Mavrilimumab 100 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 68 (42.65%)	36 / 70 (51.43%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 68 (2.94%)	0 / 70 (0.00%)	
occurrences (all)	4	0	
Hepatic enzyme increased			

subjects affected / exposed	2 / 68 (2.94%)	3 / 70 (4.29%)	
occurrences (all)	2	3	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 68 (1.47%)	3 / 70 (4.29%)	
occurrences (all)	1	3	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 68 (2.94%)	3 / 70 (4.29%)	
occurrences (all)	2	3	
Migraine			
subjects affected / exposed	0 / 68 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	0 / 68 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 68 (2.94%)	1 / 70 (1.43%)	
occurrences (all)	2	1	
Influenza like illness			
subjects affected / exposed	0 / 68 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	3	
Pyrexia			
subjects affected / exposed	2 / 68 (2.94%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 68 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 68 (1.47%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Nausea			

subjects affected / exposed	1 / 68 (1.47%)	1 / 70 (1.43%)	
occurrences (all)	2	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 68 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			
Ecchymosis			
subjects affected / exposed	1 / 68 (1.47%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 68 (1.47%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Back pain			
subjects affected / exposed	2 / 68 (2.94%)	2 / 70 (2.86%)	
occurrences (all)	3	2	
Rheumatoid arthritis			
subjects affected / exposed	2 / 68 (2.94%)	1 / 70 (1.43%)	
occurrences (all)	7	1	
Tendonitis			
subjects affected / exposed	2 / 68 (2.94%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 68 (1.47%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Ear infection			
subjects affected / exposed	1 / 68 (1.47%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Herpes simplex			
subjects affected / exposed	0 / 68 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
Influenza			
subjects affected / exposed	1 / 68 (1.47%)	1 / 70 (1.43%)	
occurrences (all)	1	1	

Nasopharyngitis			
subjects affected / exposed	1 / 68 (1.47%)	4 / 70 (5.71%)	
occurrences (all)	1	4	
Oral herpes			
subjects affected / exposed	0 / 68 (0.00%)	2 / 70 (2.86%)	
occurrences (all)	0	2	
Pharyngitis			
subjects affected / exposed	2 / 68 (2.94%)	1 / 70 (1.43%)	
occurrences (all)	2	1	
Rhinitis			
subjects affected / exposed	2 / 68 (2.94%)	1 / 70 (1.43%)	
occurrences (all)	2	1	
Upper respiratory tract infection			
subjects affected / exposed	2 / 68 (2.94%)	3 / 70 (4.29%)	
occurrences (all)	3	4	
Urinary tract infection			
subjects affected / exposed	1 / 68 (1.47%)	2 / 70 (2.86%)	
occurrences (all)	1	2	
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 68 (2.94%)	3 / 70 (4.29%)	
occurrences (all)	2	3	
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	2 / 68 (2.94%)	0 / 70 (0.00%)	
occurrences (all)	2	0	
Hypercholesterolaemia			
subjects affected / exposed	2 / 68 (2.94%)	0 / 70 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 December 2012	The maximum duration of the study was corrected from 40 weeks to 44 weeks. 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. A section describing un-blinding in the event of a suspected unexpected serious adverse reaction (SUSAR) was added to the protocol. Reference to the data safety monitoring board (DSMB) was removed from the Study-stopping Criteria section of 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. Exploratory end-point for the evaluation of flow cytometry was removed. Clarification for tuberculosis (TB) test was given if result of the QuantiFERON-TB Gold Test was indeterminate.
06 February 2013	Forced expiratory volume in 6 seconds (FEV6) assessment was added.
13 June 2013	Clinical study population was broadened to include subjects with an inadequate response to one or more conventional disease-modifying anti-rheumatic drugs (DMARDs) and anti- tumor necrosis factor (TNF) agents, clarification of forced vital capacity (FVC) was given as part of the diffusing capacity for carbon monoxide (DLCO) assessment.

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: