Clinical trial results:
A multicenter, randomized, double-blind, phase III trial to evaluate the safety, immunogenicity, and efficacy of MSB11022 compared with Humira® in patients with moderately to severely active rheumatoid arthritis

Summary

EudraCT number	2016-002852-26
Trial protocol	CZ GB HU DE LT BG
Global end of trial date	27 August 2018

Results information

Result version number	v1
This version publication date	13 July 2019
First version publication date	13 July 2019

Trial information

Trial identification

Sponsor protocol code	MS200588-0004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03052322
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Fresenius Kabi SwissBioSim GmbH
Sponsor organisation address	Route de Crassier 23 – Bâtiment A3, Eysins, Switzerland, 1262
Public contact	Andrea Rossi, Fresenius Kabi SwissBioSim GmbH, +41 79 3054454, andrea.rossi@fresenius-kabi.com
Scientific contact	Andrea Rossi, Fresenius Kabi SwissBioSim GmbH, +41 79 3054454, andrea.rossi@fresenius-kabi.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 August 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study is to evaluate the safety profile of MSB11022- modified buffer and stabilizer compared to Humira® in subjects with moderately to severely active Rheumatoid Arthritis (RA).

Protection of trial subjects:

Subject protection was ensured by following high medical and ethical standards in accordance with the principles laid down in the Declaration of Helsinki, and that are consistent with Good Clinical Practice and applicable regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 January 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 61
Country: Number of subjects enrolled	Czech Republic: 52
Country: Number of subjects enrolled	Germany: 15
Country: Number of subjects enrolled	Hungary: 23
Country: Number of subjects enrolled	Poland: 135
Country: Number of subjects enrolled	United Kingdom: 2
Worldwide total number of subjects	288
EEA total number of subjects	288

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)	241
From 65 to 84 years	47
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects were randomized in 1:1 ratio to receive either MSB11022 or EU-Humira for 48 weeks.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	MSB11022

Arm description:

Subjects received MSB11022 subcutaneously at dose of 40 milligram (mg) every other week from Day 1 up to Week 48.

Arm type	Experimental
Investigational medicinal product name	MSB11022
Investigational medicinal product code	MSB11022
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received MSB11022 subcutaneously at dose of 40 milligram (mg) every other week from Day 1 up to Week 48.

Arm title	EU-Humira

Arm description:

Subjects received EU-Humira subcutaneously at dose of 40 mg every other week from Day 1 up to Week 48.

Arm type	Active comparator
Investigational medicinal product name	EU-Humira
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received EU-Humira subcutaneously at dose of 40 mg every other week from Day 1 up to Week 48.

Number of subjects in period 1	MSB11022	EU-Humira
Started	143	145
Completed	122	113
Not completed	21	32
Consent withdrawn by subject	10	9
Adverse events	6	13
Other un-specified	1	2
Death	-	2
Lost to follow-up	2	4
Lack of efficacy	1	2
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	MSB11022
Reporting group description:	
Subjects received MSB11022 subcutaneously at dose of 40 milligram (mg) every other week from Day 1 up to Week 48.	
Reporting group title	EU-Humira
Reporting group description:	
Subjects received EU-Humira subcutaneously at dose of 40 mg every other week from Day 1 up to Week 48.	

Reporting group values	MSB11022	EU-Humira	Total
Number of subjects	143	145	288
Age categorical Units: Subjects			
Age Continuous Units: Years			
arithmetic mean	53.9	54.0	
standard deviation	± 11.9	± 11.0	-
Sex: Female, Male Units: Subjects			
Female	108	119	227
Male	35	26	61
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	2	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	142	143	285
More than one race	0	0	0
Unknown or Not Reported	1	0	1
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	3	1	4
Not Hispanic or Latino	140	144	284
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	MSB11022
Reporting group description:	
Subjects received MSB11022 subcutaneously at dose of 40 milligram (mg) every other week from Day 1 up to Week 48.	
Reporting group title	EU-Humira
Reporting group description:	
Subjects received EU-Humira subcutaneously at dose of 40 mg every other week from Day 1 up to Week 48.	

Primary: Percentage of Subjects with Treatment-emergent Adverse Events of Special Interest (AESI)

End point title	Percentage of Subjects with Treatment-emergent Adverse Events of Special Interest (AESI)[1]
End point description:	
Adverse event (AE) was defined as any untoward medical occurrence in subjects, which does not necessarily have causal relationship with treatment. Term TEAE is defined as AEs starting/worsening after first intake of the study drug. Hypersensitivity was the pre-defined TEAE of special Interest for this study. The percentage of subjects with treatment emergent AESIs (hypersensitivity) were reported. The Safety Analysis Set included all randomized subjects who received at least one dose of study treatment.	
End point type	Primary
End point timeframe:	
Up to Week 52	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be reported for this endpoint.

End point values	MSB11022	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	145		
Units: Percentage of subjects				
number (confidence interval 95%)	4.2 (1.6 to 8.9)	5.5 (2.4 to 10.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieved American College of Rheumatology 20 Response (ACR20) at Week 12

End point title	Percentage of Subjects Who Achieved American College of Rheumatology 20 Response (ACR20) at Week 12
End point description:	
ACR 20 Response: >= 20 percent improvement in swollen joint count (66 joints) & tender joint count (68 joints) & >=20 percent improvement in 3 of following 5 assessments: patient's assessment of pain using Visual Analog Scale (VAS) ; 0-10 millimeter [mm], 0=no pain & 10=worst possible pain), patient's global assessment of disease activity by using VAS (scale ranges from 0 to 100 mm, [0 mm=no pain &	

100 mm=worst possible pain]), physician's global assessment of disease activity using VAS, subjects's assessment of physical function measured by Health Assessment Questionnaire-Disability Index (HAQ-DI, defined as a 20-question instrument assessing 8 functional areas). Derived HAQ-DI ranges from 0= no difficulty & 3= inability to perform task) & acute-phase marker. Intent-To-Treat Analysis Set included all subjects randomly allocated to treatment, based on intent to treat "as randomized" principle. Here "Number of subjects analyzed" signifies those who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 12

End point values	MSB11022	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142	141		
Units: Percentage of Subjects				
number (confidence interval 95%)	79.6 (72.0 to 85.9)	80.9 (73.4 to 86.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Positive Anti-Drug Antibodies (ADAs) Status to Adalimumab

End point title	Percentage of Subjects with Positive Anti-Drug Antibodies (ADAs) Status to Adalimumab

End point description:

Percentage of subjects with positive anti-Drug antibodies (ADAs) status to Adalimumab were reported. The Safety Analysis Set included all randomized subjects who received at least one dose of study treatment. Here "n" signifies those subjects who were evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 2, 4, 12, 24, 36 and 52

End point values	MSB11022	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	145		
Units: Percentage of Subjects				
number (not applicable)				
Baseline (n= 142, 144)	7.7	4.2		
Week 2 (n= 143, 145)	20.3	15.2		
Week 4 (n= 141, 141)	29.8	21.3		
Week 12 (n= 142, 140)	54.2	48.6		
Week 24 (n= 139, 133)	71.9	61.7		
Week 36 (n= 124, 121)	66.9	65.3		
Week 52 (n= 120, 119)	60.8	62.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Drug Antibodies (ADAs) Titer Levels for Adalimumab

End point title	Anti-Drug Antibodies (ADAs) Titer Levels for Adalimumab

End point description:

Titer was defined as the degree to which the antibody-serum sample could be diluted and still contained detectable amounts of antibody. Anti-Drug Antibodies (ADAs) Titers for adalimumab was reported. Data was collected using validated bioanalytical method. The Safety Analysis Set included all randomized subjects who received at least one dose of study treatment. Here "number of subject analyzed" signifies those who were evaluable for this endpoint and "n" signifies those subjects who were evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 2, 4, 12, 24, 36 and 52

End point values	MSB11022	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	104		
Units: Titer				
median (full range (min-max))				
Baseline (n= 11, 6)	4.0 (1 to 512)	1.5 (1 to 8)		
Week 2 (n= 29, 22)	4.0 (1 to 32768)	12.0 (1 to 1024)		
Week 4 (n= 42, 30)	6.0 (1 to 16384)	6.0 (1 to 512)		
Week 12 (n= 77, 68)	16.0 (1 to 4096)	16.0 (1 to 16384)		
Week 24 (n= 100, 82)	16.0 (1 to 32768)	24.0 (1 to 131072)		
Week 36 (n= 83, 79)	16.0 (1 to 32768)	16.0 (1 to 131072)		
Week 52 (n= 73, 74)	16.0 (1 to 16384)	12.0 (1 to 32768)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Confirmed Neutralizing Antibodies (NAb) Status to Adalimumab

End point title	Percentage of Subjects with Confirmed Neutralizing Antibodies

	(NAb) Status to Adalimumab

End point description:

Percentage of subjects with confirmed neutralizing antibodies status to Adalimumab were reported. The Safety Analysis Set included all randomized subjects who received at least one dose of study treatment. Here "Number of subjects analyzed" signifies those subjects who were evaluable for this endpoint and "n" signifies those subjects who were evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 2, 4, 12, 24, 36 and 52

End point values	MSB11022	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	115	104		
Units: Percentage of Subjects				
number (not applicable)				
Baseline (n= 11, 6)	45.5	50.0		
Week 2 (n= 29, 22)	31.0	40.9		
Week 4 (n= 42, 30)	33.3	30.0		
Week 12 (n= 77, 68)	33.8	38.2		
Week 24 (n= 100, 82)	27.0	29.3		
Week 36 (n= 83, 79)	24.1	29.1		
Week 52 (n= 73, 74)	32.9	39.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieved American College of Rheumatology 20 (ACR20) Response at Week 2, 4, 8, 24 and 52

End point title	Percentage of Subjects Who Achieved American College of Rheumatology 20 (ACR20) Response at Week 2, 4, 8, 24 and 52

End point description:

ACR 20 Response: defined as greater than or equal to (>=) 20 percent improvement in swollen joint count (66 joints) and tender joint count (68 joints) and >=20 percent improvement in 3 of following 5 assessments: patient's assessment of pain using Visual Analog Scale (VAS ; 0-10 millimeter [mm], 0 mm=no pain and 10 mm=worst possible pain), patient's global assessment of disease activity by using VAS (scale ranges from 0 mm to 100 mm, [0 mm=no pain to 100 mm=worst possible pain]), physician's global assessment of disease activity using VAS, subjects's assessment of physical function measured by Health Assessment Questionnaire-Disability Index (HAQ-DI, defined as a 20-question instrument assessing 8 functional areas). derived HAQ-DI ranges from 0, indicating no difficulty, to 3, indicating inability to perform a task in that area) and acute-phase marker (CRP). ITT Analysis Set was used. Here "n" signifies those subjects who were evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Week 2, 4, 8, 24 and 52

End point values	MSB11022	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	145		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Week 2 (n= 143, 145)	30.0 (22.55 to 38.32)	29.7 (22.36 to 37.80)		
Week 4 (n= 142, 144)	52.1 (43.58 to 60.56)	52.8 (44.29 to 61.15)		
Week 8 (n= 142, 144)	71.1 (62.93 to 78.42)	72.9 (64.89 to 79.98)		
Week 24 (n= 139, 133)	88.5 (81.98 to 93.28)	83.3 (75.86 to 89.25)		
Week 52 (n= 122, 119)	81.8 (73.78 to 88.24)	86.4 (78.92 to 92.05)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieved American College of Rheumatology 50 (ACR50) Response at Week 2, 4, 8, 12, 24 and 52

End point title	Percentage of Subjects Who Achieved American College of Rheumatology 50 (ACR50) Response at Week 2, 4, 8, 12, 24 and 52

End point description:

ACR 50 Response is defined as greater than or equal to (>=) 50 percent improvement in swollen joint count (66 joints) and tender joint count (68 joints) and >=50 percent improvement in 3 of following 5 assessments: patient's assessment of pain using Visual Analog Scale (VAS ; 0-10 millimeter [mm], 0 mm=no pain and 10 mm=worst possible pain), patient's global assessment of disease activity by using VAS (scale ranges from 0 mm to 100 mm, [0 mm=no pain to 100 mm=worst possible pain]), physician's global assessment of disease activity using VAS, subjects's assessment of physical function measured by Health Assessment Questionnaire-Disability Index (HAQ-DI, defined as a 20-question instrument assessing 8 functional areas). derived HAQ-DI ranges from 0, indicating no difficulty, to 3, indicating inability to perform a task in that area) and acute-phase marker (CRP). ITT Analysis Set was used. Here "n" signifies those subjects who were evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Week 2, 4, 8, 12, 24 and 52

End point values	MSB11022	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	145		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Week 2 (n= 143, 145)	6.4 (2.9 to 11.9)	6.2 (2.9 to 11.5)		
Week 4 (n= 142, 144)	17.6 (11.7 to 24.9)	19.4 (13.3 to 26.9)		
Week 8 (n= 142, 144)	40.8 (32.7 to 49.4)	34.7 (26.9 to 43.1)		

Week 12 (n= 142, 141)	54.2 (45.7 to 62.6)	51.1 (42.5 to 59.6)		
Week 24 (n= 139, 133)	65.5 (56.9 to 73.3)	60.6 (51.7 to 68.9)		
Week 52 (n= 122, 119)	64.5 (55.3 to 72.9)	66.1 (56.8 to 74.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieved American College of Rheumatology 70 (ACR70) Response at Week 2, 4, 8, 12, 24 and 52

End point title	Percentage of Subjects Who Achieved American College of Rheumatology 70 (ACR70) Response at Week 2, 4, 8, 12, 24 and 52

End point description:

ACR 70 Response is defined as greater than or equal to (>=) 70 percent improvement in swollen joint count (66 joints) and tender joint count (68 joints) and >=70 percent improvement in 3 of following 5 assessments: patient's assessment of pain using Visual Analog Scale (VAS ; 0-10 millimeter [mm], 0 mm=no pain and 10 mm=worst possible pain), patient's global assessment of disease activity by using VAS (scale ranges from 0 mm to 100 mm, [0 mm=no pain to 100 mm=worst possible pain]), physician's global assessment of disease activity using VAS, subjects's assessment of physical function measured by Health Assessment Questionnaire-Disability Index (HAQ-DI, defined as a 20-question instrument assessing 8 functional areas). derived HAQ-DI ranges from 0, indicating no difficulty, to 3, indicating inability to perform a task in that area) and acute-phase marker (CRP). ITT Analysis Set was used. Here "n" signifies those subjects who were evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Week 2, 4, 8, 12, 24 and 52

End point values	MSB11022	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	145		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Week 2 (n= 143, 145)	0.7 (0.0 to 3.9)	0.7 (0.0 to 3.8)		
Week 4 (n= 142, 144)	4.9 (2.00 to 9.9)	2.8 (0.8 to 6.9)		
Week 8 (n= 142, 144)	14.8 (9.4 to 21.7)	12.5 (7.6 to 19.0)		
Week 12 (n= 142, 141)	26.8 (19.7 to 34.8)	19.9 (13.6 to 27.4)		
Week 24 (n= 139, 133)	33.8 (26.0 to 42.3)	35.6 (27.5 to 44.4)		
Week 52 (n= 122, 119)	39.7 (30.9 to 48.9)	42.4 (33.3 to 51.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Disease Activity Score Based on a 28 Joint Count- Erythrocyte Sedimentation Rate (DAS28-ESR) Score at Week 2, 4, 8, 12, 24 and 52

End point title	Change from Baseline in Disease Activity Score Based on a 28 Joint Count- Erythrocyte Sedimentation Rate (DAS28-ESR) Score at Week 2, 4, 8, 12, 24 and 52

End point description:

DAS calculated on 28 joints is composite score derived from 4 measures: number of swollen joints, number of tender joints, ESR, Patient's Global Assessment of Disease Activity on VAS. Overall DAS28 was derived using following formulas from DAS28: DAS28=0.56*√(TJC28)+0.28*√(SJC28) +0.014*GH+0.70*ln(ESR). Where: TJC28 = 28 joint count for tenderness, SJC28 = 28 joint count for swelling, ln(ESR) = natural log of ESR, GH = general health component of DAS (ie, Patient's Global Assessment of Disease Activity, assessed using scale of 1-100 where 100 is maximal activity; For analyses, GH divided by 10 & converted to a 0.5 scale, i.e., 0, 0.5, 1, 1.5. DAS28-ESR of >5.1 implies active disease, <3.2 low disease activity, & <2.6 remission. Change of 1.2(twice measurement error)= significant change of disease activity state. Overall score ranges from 0-10 where higher score means more severe disease. ITT Analysis Set used. Here "n"= subjects evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 2, 4, 8, 12, 24 and 52

End point values	MSB11022	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	145		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change at Week 2 (n= 140, 145)	-0.9 (± 0.9)	-0.7 (± 0.9)		
Change at Week 4 (n= 141, 144)	-1.4 (± 1.1)	-1.2 (± 1.0)		
Change at Week 8 (n= 142, 144)	-1.9 (± 0.9)	-1.7 (± 1.1)		
Change at Week 12 (n= 142, 141)	-2.4 (± 1.1)	-2.1 (± 1.2)		
Change at Week 24 (n= 138, 132)	-2.7 (± 1.0)	-2.3 (± 1.2)		
Change at Week 52 (n= 121, 118)	-2.8 (± 1.1)	-2.5 (± 1.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Disease Activity Score Based on 28-joints Count- Erythrocyte Sedimentation Rate (DAS28-ESR) low Disease Activity and Remission at Week 2, 4, 8, 12, 24, and 52

End point title	Percentage of Subjects with Disease Activity Score Based on 28-joints Count- Erythrocyte Sedimentation Rate (DAS28-ESR) low Disease Activity and Remission at Week 2, 4, 8, 12, 24, and 52

End point description:

Disease Activity Score calculated on 28 joints is composite score derived from 4 measures: number of swollen joints (out of 28), -number of tender joints (out of 28), -Erythrocyte sedimentation rate (ESR), -Patient's Global Assessment of Disease Activity on visual analog scale (VAS). Overall disease activity

score DAS28 was derived using following formulas from DAS28: DAS28=0.56*√(TJC28)+0.28*√(SJC28) + 0.014*GH+0.70*ln(ESR). Where: -TJC28 = 28 joint count for tenderness, -SJC28 = 28 joint count for swelling, -ln(ESR) = natural logarithm of ESR, -GH = general health component of DAS (ie, Patient's Global Assessment of Disease Activity, assessed using scale of 1 to 100 where 100 is maximal activity; For analyses, GH was divided by 10 and converted to a 0.5 scale, i.e., 0, 0.5, 1, 1.5. DAS28-ESR of >5.1 implies active disease, <3.2 low disease activity, and <2.6 remission. ITT Analysis Set used. Here "n" = subjects who were evaluable for this endpoint at

End point type	Secondary

End point timeframe:

Week 2, 4, 8, 12, 24, and 52

End point values	MSB11022	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	145		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Low Disease Activity: Week 2 (n= 143, 145)	10.0 (5.6 to 16.2)	8.3 (4.4 to 14.0)		
Low Disease Activity: Week 4 (n= 142, 144)	20.6 (14.2 to 28.2)	16.0 (10.4 to 23.0)		
Low Disease Activity: Week 8 (n= 142, 144)	33.1 (25.4 to 41.5)	33.3 (25.7 to 41.7)		
Low Disease Activity: Week 12 (n= 142, 141)	46.5 (38.1 to 55.0)	42.6 (34.3 to 51.2)		
Low Disease Activity: Week 24 (n= 139, 133)	55.1 (46.4 to 63.5)	53.8 (44.9 to 62.5)		
Low Disease Activity: Week 52 (n= 122, 119)	57.0 (47.7 to 65.9)	56.8 (47.3 to 65.9)		
Remission: Week 2 (n= 143, 145)	3.6 (1.2 to 8.1)	2.1 (0.4 to 5.9)		
Remission: Week 4 (n= 142, 144)	7.8 (3.9 to 13.5)	6.9 (3.4 to 12.4)		
Remission: Week 8 (n= 142, 144)	18.3 (12.3 to 25.7)	16.0 (10.4 to 23.0)		
Remission: Week 12 (n= 142, 141)	29.6 (22.2 to 37.8)	24.1 (17.3 to 32.0)		
Remission: Week 24 (n= 139, 133)	31.2 (23.6 to 39.6)	34.1 (26.1 to 42.8)		
Remission: Week 52 (n= 122, 119)	40.5 (31.7 to 49.8)	36.4 (27.8 to 45.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Simplified Disease Activity Index (SDAI) Total Score at Week 2, 4, 8, 12, 24, and 52

End point title	Change from Baseline in Simplified Disease Activity Index (SDAI) Total Score at Week 2, 4, 8, 12, 24, and 52

End point description:

SDAI is numerical sum of 5 parameters: tender & swollen joint count, Patient's & Physician's Global Assessment of Disease Activity (VAS) & level of C-reactive protein (CRP) (mg/dL), normal<1 mg/dL. SDAI was calculated based on following formula: SDAI = 28 joint count for swelling (SJC28) + 28 joint for tenderness (TJC28)+GH+PGA+CRP Where: GH =general health component of DAS (i.e. Patient's

Global Assessment of Disease Activity, assessed using scale of 1 to 100, here 100 is maximal activity. GH was divided by 10 & converted to 0.5 scale (0, 0.5, 1, 1.5).-PGA = Physician's Global Assessment of Disease Activity assessed using scale of 1 to 100 where 100 is maximal activity. For analyses, PGA was divided by 10 & converted to 0.5 scale (0, 0.5, 1, 1.5). where [0-0.25=0, [0.25-0.75]=0.5, [0.76-1.25]=1. Total score range was 0-86 & lower score indicates less disease activity. ITT Analysis Set used. Here "n" signifies subjects who were evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 2, 4, 8, 12, 24, and 52

End point values	MSB11022	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	145		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change at Week 2 (n= 139, 145)	-11.5 (± 10.6)	-9.1 (± 10.0)		
Change at Week 4 (n= 140, 140)	-18.0 (± 11.3)	-16.0 (± 10.9)		
Change at Week 8 (n= 141, 144)	-24.0 (± 10.6)	-21.4 (± 11.0)		
Change at Week 12 (n= 140, 141)	-27.9 (± 10.8)	-24.7 (± 10.9)		
Change at Week 24 (n= 136, 131)	-31.4 (± 11.2)	-27.8 (± 10.6)		
Change at Week 52 (n= 118, 118)	-31.5 (± 11.6)	-29.1 (± 10.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Clinical Disease Activity Index (CDAI) Total Score at Week 2, 4, 8, 12, 24 and 52

End point title	Change From Baseline in Clinical Disease Activity Index (CDAI) Total Score at Week 2, 4, 8, 12, 24 and 52

End point description:

Clinical Disease Activity Index (CDAI) is a composite index (without acute-phase reactant) for assessing disease activity. CDAI was calculated based on following formula: CDAI = 28 joint count for swelling (SJC28) + 28 joint count for tenderness (TJC28) + GH + PGA. Where, -GH = general health component of DAS (i.e., Patient's Global Assessment of Disease Activity, assessed using a scale of 1 to 100 where 100 is maximal activity; GH was divided by 10 & converted to a 0.5 scale, i.e., 0, 0.5, 1, 1.5 etc. where [0-0.25] = 0,[0.25-0.75] = 0.5, [0.76-1.25] = 1, etc.). -PGA = Physician's Global Assessment of Disease Activity assessed using a scale of 1 to 100 where 100 is maximal activity. PGA was divided by 10 & converted to a 0.5 scale, ie, 0, 0.5, 1, 1.5 etc. where [0-0.25] = 0, [0.25-0.75] = 0.5, [0.76-1.25] = 1. CDAI ranges from 0 to 76. Lower score indicates less disease activity. ITT Analysis Set used. Here "n"= subjects who were evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 2, 4, 8, 12, 24 and 52

End point values	MSB11022	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	145		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change at Week 2 (n= 139, 145)	-10.8 (± 10.3)	-8.5 (± 9.9)		
Change at Week 4 (n= 141, 144)	-17.4 (± 11.2)	-15.2 (± 10.7)		
Change at Week 8 (n= 141, 144)	-23.5 (± 10.6)	-20.6 (± 10.9)		
Change at Week 12 (n= 141, 141)	-27.4 (± 10.5)	-24.1 (± 10.7)		
Change at Week 24 (n= 138, 132)	-30.8 (± 10.9)	-27.1 (± 10.7)		
Change at Week 52 (n= 120, 118)	-31.1 (± 11.2)	-28.5 (± 10.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) Boolean Remission at Week 2, 4, 8, 12, 24 and 52

End point title	Percentage of Subjects With American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) Boolean Remission at Week 2, 4, 8, 12, 24 and 52

End point description:

According to Boolean-based definition of remission of ACR/EULAR, a Subjects must satisfy all of the following: tender joint count <= 1, swollen joint count <= 1, CRP <= 1 mg/dL, and Patient's Global Assessment of Disease Activity <= 1 (0 to 10 VAS). Physician's Global Assessment of Disease Activity (PGA) was assessed on a 10 mm VAS ranging from 0 (very well) to 10 (very poor), where higher scores indicate worse health condition. Here "n" signifies those subjects who were evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Week 2, 4, 8, 12, 24 and 52

End point values	MSB11022	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	145		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Week 2 (n= 143, 145)	0.7 (0.0 to 3.9)	0.0 (0.0 to 2.5)		
Week 4 (n= 142, 144)	0.7 (0.0 to 3.9)	1.4 (0.8 to 5.1)		
Week 8 (n= 142, 144)	3.5 (1.2 to 8.0)	4.2 (1.5 to 8.9)		
Week 12 (n= 142, 141)	5.7 (2.5 to 10.9)	12.1 (7.2 to 18.6)		
Week 24 (n= 139, 133)	11.7 (6.8 to 18.3)	8.4 (4.3 to 14.5)		
Week 52 (n= 122, 119)	21.0 (14.1 to 29.4)	13.6 (7.9 to 21.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs and TEAEs Leading to Death

End point title	Percentage of Subjects With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs and TEAEs Leading to Death

End point description:

Adverse event(AE) was defined as any untoward medical occurrence in participants which does not necessarily have causal relationship with treatment. A serious adverse event(SAE) was AE that resulted in any of the following outcomes: death; life threatening; persistent/significant disability/incapacity; initial/prolonged inpatient hospitalization; congenital anomaly/birth defect or was otherwise considered medically important. Term TEAE is defined as AEs starting/worsening after first intake of the study drug. All abnormal physical examinations occurring during the study have been reported as Adverse events. TEAEs included both Serious TEAEs and non-serious TEAEs. The Safety Analysis Set included all randomized subjects who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Week 69

End point values	MSB11022	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	145		
Units: Percentage of Subjects				
number (not applicable)				
TEAEs	58.0	64.1		
Serious TEAEs	5.6	9.7		
TEAEs Leading to Death	0	0.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinically Meaningful Differences in Vital Signs

End point title	Percentage of Subjects With Clinically Meaningful Differences in Vital Signs

End point description:

Vital signs including body temperature, respiratory rate, and heart rate (after 5-minute rest) were measured. Percentage of subjects with clinically meaningful abnormalities in vital signs were reported. Clinical meaningful was determined by the investigator. The Safety Analysis Set included all randomized subjects who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	MSB11022	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	145		
Units: Percentage of Subjects				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinically Meaningful Differences in Laboratory values

End point title	Percentage of Subjects With Clinically Meaningful Differences in Laboratory values

End point description:

Laboratory parameters including hematology, urinalysis, and biochemistry analysis were analyzed. The Safety Analysis Set included all randomized subjects who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	MSB11022	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	145		
Units: Percentage of Subjects				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinically Significant Abnormal Values for 12-lead Electrocardiogram (ECG) at Week 12, 24, and 52

End point title	Percentage of Subjects With Clinically Significant Abnormal Values for 12-lead Electrocardiogram (ECG) at Week 12, 24, and 52

End point description:

Percentage of subjects with clinically significant abnormal values for 12-lead electrocardiogram (ECG) at

week 12, 24, and 52 were reported. Here "n" signifies those subjects who were evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Week 12, 24, and 52

End point values	MSB11022	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	145		
Units: Percentage of Subjects				
number (not applicable)				
Week 12 (n= 142, 141)	0	0		
Week 24 (n= 139, 133)	0	1.5		
Week 52 (n= 122, 119)	0	0.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Anti-Nuclear Antibody (ANA) and Anti double-stranded Deoxyribonucleic acid (Anti-dsDNA) at Baseline, Week 24 and 52

End point title	Percentage of Subjects With Anti-Nuclear Antibody (ANA) and Anti double-stranded Deoxyribonucleic acid (Anti-dsDNA) at Baseline, Week 24 and 52

End point description:

For ANA, positivity is defined as any subject with ANA titer greater than (>) 1:160 and negativity is defined as ANA titer less than (<) 1:160. For anti-ds DNA, positivity is defined as any subject with adsDNA > 15 units per milliliter (U/mL), intermediate category is defined as value between 10 U/mL to 15 U/mL and negativity is defined as adsDNA < 10 U/mL. Percentage of subjects with anti-nuclear antibody (ANA) and anti double-stranded deoxyribonucleic acid (Anti-dsDNA) at baseline, week 24 and 52 were reported. Here "n" signifies those subjects who were evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 24 and 52

End point values	MSB11022	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	145		
Units: Percentage of Subjects				
number (not applicable)				
Baseline: ANA: Negative (n= 143, 145)	97.2	95.1		
Baseline: ANA: Positive (n= 143, 145)	2.8	4.9		
Week 24: ANA: Negative (n= 138, 131)	92.0	91.6		
Week 24: ANA: Positive (n= 138, 131)	8.0	8.4		
Week 52: ANA: Negative (n= 118, 111)	78.8	84.7		

Week 52: ANA: Positive (n= 118, 111)	21.2	15.3		
Baseline: Anti-dsDNA: Negative (n= 141, 141)	97.9	98.6		
Baseline: Anti-dsDNA: Intermediate (n= 141, 141)	1.4	0.7		
Baseline: Anti-dsDNA: Positive (n= 141, 141)	0.7	0.7		
Week 24: Anti-dsDNA: Negative (n= 138, 132)	95.7	96.2		
Week 24: Anti-dsDNA: Intermediate (n= 138, 132)	2.2	3.0		
Week 24: Anti-dsDNA: Positive (n= 138, 132)	2.2	0.8		
Week 52: Anti-dsDNA: Negative (n= 121, 118)	95.0	97.5		
Week 52: Anti-dsDNA: Intermediate (n= 121, 118)	0.8	1.7		
Week 52: Anti-dsDNA: Positive (n= 121, 118)	4.1	0.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Health assessment questionnaire disability index (HAQ-DI) Total Score at Baseline, Weeks 12, 24 and 52

End point title	Health assessment questionnaire disability index (HAQ-DI) Total Score at Baseline, Weeks 12, 24 and 52

End point description:

The HAQ-DI is a participant-reported questionnaire that is commonly used in RA to measure disease associated disability (assessment of physical function). It consists of several questions referring to 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and activities. HAQ-DI scores range from 0 to 3. The disability section of the questionnaire scores the participant's self-perception on the degree of difficulty (0 = without any difficulty, 1 = with some difficulty, 2 = with much difficulty, and 3 = unable to do). ITT analysis set was used. Here "n" signifies those subjects who were evaluable for this endpoint at specified time
points.

End point type	Secondary

End point timeframe:

Baseline, Weeks 12, 24 and 52

End point values	MSB11022	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	145		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n= 143, 145)	1.6 (± 0.6)	1.6 (± 0.6)		
Week 12 (n= 142, 141)	1.1 (± 0.6)	1.1 (± 0.6)		
Week 24 (n= 139, 132)	1.0 (± 0.6)	1.0 (± 0.6)		
Week 52 (n= 121, 118)	0.9 (± 0.7)	0.9 (± 0.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Short-Form Health Survey- 36 Items (SF-36) at Baseline, Week 12, 24 and 52

End point title	Short-Form Health Survey- 36 Items (SF-36) at Baseline, Week 12, 24 and 52

End point description:

SF-36: Validated 36-item, patient-reported indication of overall health status not specific to any age, disease/Treatment group. SF-36 questionnaire contains 36 questions pertaining to eight subscales of health status. 8 subscales summarized as relating to either physical health/mental health. Physical component summary (PCS): based primarily on physical functioning, role-physical, bodily pain & general health scales & mental component summary(MCS): vitality, social functioning, role-emotional & mental health scales. Score from mental health, role emotional, social functioning & vitality domains averaged to calculate MCS.Total score range for MCS: 0-100(100=highest level of mental functioning). Score from physical function, role physical, bodily pain & general health domains averaged to calculate PCS. Total score range for PCS: 0-100(100=highest level of physical functioning). ITT analysis set used. Here "n" signifies those subjects who evaluable for this endpoint at specified time.

End point type	Secondary

End point timeframe:

Baseline, Week 12, 24 and 52

End point values	MSB11022	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	145		
Units: Units on a scale				
arithmetic mean (standard deviation)				
PCS: Baseline (n= 134, 134)	30.3 (± 7.6)	30.6 (± 7.8)		
PCS: Week 12 (n= 142, 141)	39.0 (± 7.9)	38.6 (± 8.6)		
PCS: Week 24 (n= 139, 132)	40.5 (± 8.8)	40.9 (± 9.1)		
PCS: Week 52 (n= 121, 118)	41.8 (± 9.5)	41.6 (± 9.3)		
MCS: Baseline (n= 134, 134)	40.9 (± 13.2)	43.4 (± 11.7)		
MCS: Week 12 (n= 142, 141)	47.4 (± 11.3)	48.2 (± 11.3)		
MCS: Week 24 (n= 139, 132)	49.8 (± 10.8)	48.8 (± 10.9)		
MCS: Week 52 (n= 121, 118)	48.0 (± 10.4)	49.3 (± 11.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Euro-Quality of Life - 5 dimension-5 levels (EQ-5D-5L) Utility Index

Score at Baseline, Week 12, 24 and 52

End point title	Euro-Quality of Life - 5 dimension-5 levels (EQ-5D-5L) Utility Index Score at Baseline, Week 12, 24 and 52

End point description:

EQ-5D-5L: standardized, participant-rated questionnaire to assess health-related quality of life. EQ-5D-5L includes 2 components: EQ-5D-5L health state profile & EQ-5D-5L VAS. EQ-5D-5L descriptive system provides a profile of participant's health state 5 dimensions: mobility, self-care, usual activities, pain/discomfort & anxiety/depression. Each dimension has 5 response options (no problems, slight problems, moderate problems, severe problems & extreme problems) that reflect increasing levels of difficulty. Participant was asked to indicate his/her current health state by selecting most appropriate level in each of 5 dimensions. Responses to 5 dimension scores were combined & converted into single preference-weighted health utility index score 0(0.0- worst health state) to 1(1.0- better health state) representing general health status of individual based on UK scoring algorithm. ITT analysis set used. Here "n"= subjects who were evaluable for this endpoint at specified time point.

End point type	Secondary

End point timeframe:

Baseline, Week 12, 24 and 52

End point values	MSB11022	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	145		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n= 134, 133)	0.6 (± 0.2)	0.6 (± 0.2)		
Week 12 (n= 142, 140)	0.8 (± 0.1)	0.8 (± 0.1)		
Week 24 (n= 139, 132)	0.8 (± 0.1)	0.8 (± 0.1)		
Week 52 (n= 121, 118)	0.8 (± 0.22)	0.8 (± 0.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Euro-Quality of Life - 5 dimension-5 levels (EQ-5D-5L) Visual Analogue Scale (VAS) Score at Baseline, Week 12, 24 and 52

End point title	Euro-Quality of Life - 5 dimension-5 levels (EQ-5D-5L) Visual Analogue Scale (VAS) Score at Baseline, Week 12, 24 and 52

End point description:

EQ-5D-5L: Standardized, participant-rated questionnaire to assess health-related quality of life. EQ-5D-5L includes 2 components: EQ-5D-5L health state profile & EQ-5D-5L VAS. EQ-5D-5L descriptive system provides a profile of participant's health state 5 dimensions: mobility, self-care, usual activities, pain/discomfort & anxiety/depression. Each dimension has 5 responses (no problems, slight problems, moderate problems, severe problems & extreme problems) that reflect increasing levels of difficulty. Responses to 5 dimension scores combined & converted into single preference-weighted health utility index score 0(worst health) to 1 (better health). EQ-VAS: Self-rated health status using a vertical VAS. EQ-VAS records participant's perceptions of their own current overall health in range from 0(worst imaginable health)-100(best imaginable health). ITT analysis set used. Here "n" signifies subjects evaluable for this endpoint at specified time point.

End point type	Secondary

End point timeframe:

Baseline, Week 12, 24 and 52

End point values	MSB11022	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	145		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline (n= 134, 133)	42.4 (± 18.5)	45.4 (± 20.4)		
Week 12 (n= 142, 140)	64.6 (± 19.6)	63.2 (± 20.9)		
Week 24 (n= 139, 132)	66.2 (± 22.2)	65.6 (± 24.3)		
Week 52 (n= 121, 118)	68.8 (± 21.7)	69.0 (± 22.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline (Week 4) in Injection Site Pain as Assessed by Visual Analogue Scale (VAS) at Week 6 and 8

End point title	Mean Change From Baseline (Week 4) in Injection Site Pain as Assessed by Visual Analogue Scale (VAS) at Week 6 and 8

End point description:

The participant's reported perception of pain was measured on a VAS where the slash drawn by the participant represents pain of increasing intensity. VAS score ranges from 0-10 millimeter [mm], where; 0 mm=no pain and 10 mm=worst possible pain. The first 2 injections was administered by qualified personnel. The next three doses of Investigational Medicinal Products (IMPs) (3-5) will be self-administered by the participant and injection site pain was assessed. Pain was recorded immediately after, 15 minutes after, and 1 hour after the injections received by the participants. The Safety Analysis Set included all randomized subjects who received at least one dose of study treatment. Here "n" signifies those subjects who were evaluable for this endpoint at specified time points.

End point type	Secondary

End point timeframe:

Immediately, 15 minutes and 1 hour post-injection on Baseline (Week 4), Week 6 and 8

End point values	MSB11022	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	143	145		
Units: Millimeter (mm)				
arithmetic mean (standard deviation)				
Week 4: Immediately post-injection (n= 140, 143)	3.0 (± 8.4)	6.4 (± 14.3)		
Week 4: 15 min post-injection (n= 140, 143)	0.6 (± 2.5)	1.7 (± 7.6)		
Week 4: 1 hour post-injection (n= 140, 143)	0.1 (± 0.6)	0.8 (± 5.6)		
Change:Week6:Immediately post-injection(n=140,143)	-1.4 (± 5.1)	-1.3 (± 10.2)		
Change:Week 6:15 min post-injection (n= 140, 143)	-0.2 (± 2.7)	0.4 (± 3.3)		

Change: Week 6:1 hour post-injection (n= 140, 143)	0.0 (± 0.7)	0.0 (± 2.7)		
Change:Week8:Immediately post-injection(n=140,139)	-1.7 (± 6.5)	-2.3 (± 10.4)		
Change:Week 8:15 min post-injection (n= 140, 139)	-0.3 (± 2.3)	-0.7 (± 4.1)		
Change:Week 8: 1 hour post-injection (n= 140, 139)	-0.1 (± 0.6)	-0.7 (± 5.4)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to Week 69	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups	
Reporting group title	EU-Humira
Reporting group description:	
Participants received EU-Humira subcutaneously at dose of 40 mg every other week from Day 1 up to Week 48.	
Reporting group title	MSB11022
Reporting group description:	
Participants received MSB11022 subcutaneously at dose of 40 milligram (mg) every other week from Day 1 up to Week 48.	

Serious adverse events	EU-Humira	MSB11022	
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 145 (10.34%)	8 / 143 (5.59%)	
number of deaths (all causes)	2	0	
number of deaths resulting from adverse events			
Investigations			
Mycobacterium tuberculosis complex test positive			
subjects affected / exposed	1 / 145 (0.69%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Arteriosclerosis coronary artery			
subjects affected / exposed	1 / 145 (0.69%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 145 (0.69%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			

subjects affected / exposed	1 / 145 (0.69%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
Transient global amnesia			
subjects affected / exposed	0 / 145 (0.00%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 145 (0.69%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 145 (0.00%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 145 (0.69%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Rheumatoid lung			
subjects affected / exposed	1 / 145 (0.69%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 145 (0.69%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			

Osteoarthritis			
subjects affected / exposed	2 / 145 (1.38%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid arthritis			
subjects affected / exposed	2 / 145 (1.38%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical spinal stenosis			
subjects affected / exposed	0 / 145 (0.00%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovial cyst			
subjects affected / exposed	0 / 145 (0.00%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	1 / 145 (0.69%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 145 (0.69%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection viral			
subjects affected / exposed	1 / 145 (0.69%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheobronchitis			
subjects affected / exposed	1 / 145 (0.69%)	0 / 143 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			

subjects affected / exposed	0 / 145 (0.00%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device dislocation			
subjects affected / exposed	0 / 145 (0.00%)	1 / 143 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	EU-Humira	MSB11022	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 145 (23.45%)	15 / 143 (10.49%)	
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	12 / 145 (8.28%)	4 / 143 (2.80%)	
occurrences (all)	93	4	
Injection site pain			
subjects affected / exposed	10 / 145 (6.90%)	2 / 143 (1.40%)	
occurrences (all)	25	2	
Injection site pruritus			
subjects affected / exposed	8 / 145 (5.52%)	1 / 143 (0.70%)	
occurrences (all)	55	1	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	8 / 145 (5.52%)	2 / 143 (1.40%)	
occurrences (all)	38	20	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	13 / 145 (8.97%)	6 / 143 (4.20%)	
occurrences (all)	14	6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 July 2017	- Administrative and editorial changes were undertaken to correct typographical errors that do not impact the design or execution of the study

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported