Clinical trial results:
A Randomized, Double-blind, Confirmatory Trial to Evaluate the Efficacy, Safety, and Immunogenicity of MSB11022 Compared with European Union-approved Humira® in Subjects with Moderate to Severe Chronic Plaque Psoriasis

Summary

EudraCT number	2015-003287-37
Trial protocol	BG DE GB CZ HU
Global end of trial date	18 December 2017

Results information

Result version number	v1
This version publication date	25 October 2018
First version publication date	25 October 2018

Trial information

Trial identification

Sponsor protocol code	EMR200588-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02660580
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck KGaA
Sponsor organisation address	Frankfurter Strasse 250, Darmstadt, Germany, 64293
Public contact	Merck KGaA, Communication Centre Merck KGaA, +49 6151725200, service@merckgroup.com
Scientific contact	Merck KGaA, Communication Centre Merck KGaA, +49 6151725200, service@merckgroup.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	18 December 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 December 2016
Global end of trial reached?	Yes
Global end of trial date	18 December 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to demonstrate equivalence in efficacy of MSB11022 compared to EU-approved Humira in subjects with moderate to severe chronic plaque psoriasis.

Protection of trial subjects:

Subject protection was ensured by following high medical and ethical standards in accordance with the ethical principles of the International Council for Harmonisation (ICH) guideline for Good Clinical Practice (GCP) and the Declaration of Helsinki, as well as with applicable local regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 February 2016
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: 34
Country: Number of subjects enrolled	Canada: 51
Country: Number of subjects enrolled	Czech Republic: 57
Country: Number of subjects enrolled	Estonia: 41
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 20
Country: Number of subjects enrolled	Hungary: 19
Country: Number of subjects enrolled	Mexico: 31
Country: Number of subjects enrolled	Poland: 156
Country: Number of subjects enrolled	Russian Federation: 24
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	United States: 6
Worldwide total number of subjects	443
EEA total number of subjects	331

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)	422
From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects were randomized to receive either MSB11022 or EU-Humira in Core Treatment Period till Week 16. Subjects who achieved PASI 50 at Week 16 entered Extension Period where subjects in MSB11022 arm were continued to receive MSB11022 and subjects in EU-Humira arm were re-randomized to receive either MSB11022 or EU-Humira for additional 37 weeks.

Period 1

Period 1 title	Core Treatment Period (Week 1 to 16)
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 (Core Treatment Period)

Arm description:

Subjects received MSB11022 subcutaneously at an initial dose of 80 milligram (mg) on Day 1 of Week 1 followed by 40 mg every other week starting at Week 2 up to and including Week 14 in Core Treatment Period.

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

Dosage and administration details:

Subjects received MSB11022 subcutaneously at an initial dose of 80 mg on Day 1 of Week 1 followed by 40 mg every other week starting at Week 2 up to and including Week 14.

Arm title	EU-Humira

Arm description:

Subjects received EU-Humira subcutaneously at an initial dose of 80 mg on Day 1 of Week 1 followed by 40 mg every other week starting at Week 2 up to and including Week 14 in Core Treatment Period.

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 an initial dose of 80 mg on Day 1 of Week 1 followed by 40 mg every other week starting at Week 2 up to and including Week 14.

Number of subjects in period 1	MSB11022 (Core Treatment Period)	EU-Humira
Started	222	221
Treated	221	220
Completed	213	202
Not completed	9	19
Consent withdrawn by subject	1	4
Adverse events	2	9
Other un-specified	1	-
Lost to follow-up	1	2
Randomized, not treated	1	1
Protocol deviation	3	1
Lack of efficacy	-	2

Period 2

Period 2 title	Extended Treatment Period(Week 16 to 52)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	MSB11022 (Extended Treatment Period)

Arm description:

Subjects who had achieved PASI 50 and received MSB11022 during Core Treatment Period continued to receive MSB11022 subcutaneously at dose of 40 mg every other week starting at Week 16 up to and including Week 50 in extended treatment period.

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

Dosage and administration details:

Subjects who received MSB11022 during core treatment period continued to receive MSB11022 subcutaneously at dose of 40 mg every other week starting at Week 16 up to and including Week 50 in extended treatment period.

Arm title	EU-Humira/EU-Humira

Arm description:

Subjects who had achieved PASI 50 and received EU-Humira in Core Treatment Period and continued to receive EU-Humira subcutaneously at dose of 40 mg every other week starting at Week 16 up to and including Week 50 after re-randomization in extended treatment period.

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 who received EU-Humira in core treatment period and continued to receive EU-Humira subcutaneously at dose of 40 mg every other week starting at Week 16 up to and including Week 50 after re-randomization in extended treatment period.

Arm title	EU-Humira/MSB11022

Arm description:

Subjects who had achieved PASI 50 and received EU-Humira in Core Treatment Period were re-randomized to receive MSB11022 subcutaneously at dose of 40 mg every other week starting at Week 16 up to and including Week 50 in extended treatment period.

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

Dosage and administration details:

Subjects who received EU-Humira in core treatment period were re-randomized to receive MSB11022 subcutaneously at dose of 40 mg every other week starting at Week 16 up to and including Week 50 in extended treatment period.

Number of subjects in period 2	MSB11022 (Extended Treatment Period)	EU-Humira/EU-Humira	EU-Humira/MSB11022
Started	213	101	101
Completed	195	90	90
Not completed	18	11	11
Consent withdrawn by subject	3	2	2
Adverse events	8	6	4
Other un-specified	1	-	1
Lost to follow-up	-	1	1
Lack of efficacy	4	2	2
Protocol deviation	2	-	1

Baseline characteristics

Reporting groups	
Reporting group title	MSB11022 (Core Treatment Period)
Reporting group description:	
Subjects received MSB11022 subcutaneously at an initial dose of 80 milligram (mg) on Day 1 of Week 1 followed by 40 mg every other week starting at Week 2 up to and including Week 14 in Core Treatment Period.	
Reporting group title	EU-Humira
Reporting group description:	
Subjects received EU-Humira subcutaneously at an initial dose of 80 mg on Day 1 of Week 1 followed by 40 mg every other week starting at Week 2 up to and including Week 14 in Core Treatment Period.	

Reporting group values	MSB11022 (Core Treatment Period)	EU-Humira	Total
Number of subjects	222	221	443
Age Categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	44.5	42.7	
standard deviation	± 12.8	± 12.0	-
Gender Categorical Units: Subjects			
Female	75	73	148
Male	147	148	295
Race Units: Subjects			
White	205	200	405
Black or African American	2	1	3
Asian	5	9	14
American Indian or Alaska Native	10	8	18
Native Hawaiian or Other Pacific Islander	0	0	0
Other	0	1	1
Missing/Not collected at this site	0	2	2
Ethnicity Units: Subjects			
Hispanic or Latino	23	23	46
Not Hispanic or Latino	199	196	395
Missing	0	2	2

End points

End points reporting groups

Reporting group title	MSB11022 (Core Treatment Period)

Reporting group description:

Subjects received MSB11022 subcutaneously at an initial dose of 80 milligram (mg) on Day 1 of Week 1 followed by 40 mg every other week starting at Week 2 up to and including Week 14 in Core Treatment Period.

Reporting group title	EU-Humira

Reporting group description:

Subjects received EU-Humira subcutaneously at an initial dose of 80 mg on Day 1 of Week 1 followed by 40 mg every other week starting at Week 2 up to and including Week 14 in Core Treatment Period.

Reporting group title	MSB11022 (Extended Treatment Period)

Reporting group description:

Subjects who had achieved PASI 50 and received MSB11022 during Core Treatment Period continued to receive MSB11022 subcutaneously at dose of 40 mg every other week starting at Week 16 up to and including Week 50 in extended treatment period.

Reporting group title	EU-Humira/EU-Humira

Reporting group description:

Subjects who had achieved PASI 50 and received EU-Humira in Core Treatment Period and continued to receive EU-Humira subcutaneously at dose of 40 mg every other week starting at Week 16 up to and including Week 50 after re-randomization in extended treatment period.

Reporting group title	EU-Humira/MSB11022

Reporting group description:

Subjects who had achieved PASI 50 and received EU-Humira in Core Treatment Period were re-randomized to receive MSB11022 subcutaneously at dose of 40 mg every other week starting at Week 16 up to and including Week 50 in extended treatment period.

Subject analysis set title	MSB11022 (Overall Treatment Period)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received MSB11022 subcutaneously at dose of 40 mg every other week starting at Week 1 up to and including Week 50 in overall treatment period.

Subject analysis set title	EU-Humira/EU-Humira (Overall Treatment Period)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects who received EU-Humira up to Week 16 continued to receive EU-Humira subcutaneously at dose of 40 mg every other week starting at Week 16 up to and including Week 50 after re-randomization in overall treatment period.

Subject analysis set title	EU-Humira/MSB11022 (Overall Treatment Period)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects who received EU-Humira up to Week 16 were re-randomized to receive MSB11022 subcutaneously at dose of 40 mg every other week starting at Week 16 up to and including Week 50 in overall treatment period.

Primary: Percentage of Subjects Who Achieved Psoriasis Area and Severity Index 75 (PASI 75) at Week 16

End point title	Percentage of Subjects Who Achieved Psoriasis Area and Severity Index 75 (PASI 75) at Week 16

End point description:

PASI correlates to the physician's assessment of psoriasis symptoms including redness of lesions, thickness of lesions, scaliness of lesions and extent of disease. Each parameter is graded from 0-4, 0 refers to no disease and 4 to severe involvement. The body is divided into 4 areas for scoring (head, arms, trunk to groin, legs to top of buttocks), and the final score ranges from 0-72 with higher scores reflecting more disease severity. The PASI-75 response is defined as the percentage of subjects who achieved at least a 75% improvement in PASI score from Baseline. The per-protocol (PP) Analysis Set included all randomized and treated subjects who did not have any major protocol deviations during the

Core Treatment Period with respect to factors likely to affect the efficacy of treatment.

End point type	Primary

End point timeframe:

Week 16

End point values	MSB11022 (Core Treatment Period)	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	191		
Units: Percentage of Subjects				
number (not applicable)	89.7	91.6		

Statistical analyses

Statistical analysis title	Percentage of Subjects With PASI-75
Comparison groups	MSB11022 (Core Treatment Period) v EU-Humira
Number of subjects included in analysis	394
Analysis specification	Pre-specified
Analysis type	equivalence[1]
Parameter estimate	Percentage difference
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.82
upper limit	4.07

Notes:

[1] - MSB11022 was considered equivalent to EU-Humira if the 95% stratified Newcombe Confidence Interval (CI) for the difference in percentage was included in the equivalence interval (-18, 18).

Secondary: Percent Change From Baseline in PASI at Week 16

End point title	Percent Change From Baseline in PASI at Week 16

End point description:

PASI correlates to the physician's assessment of psoriasis symptoms including redness of lesions, thickness of lesions, scaliness of lesions and extent of disease. Each parameter is graded from 0-4, 0 refers to no disease and 4 to severe involvement. The body is divided into 4 areas for scoring (head, arms, trunk to groin, legs to top of buttocks), and the final score ranges from 0-72, with higher scores reflecting more disease severity. Percent change from Baseline in PASI score was reported. The PP Analysis set was used.

End point type	Secondary

End point timeframe:

Baseline (Core Treatment Period), Week 16

End point values	MSB11022 (Core Treatment Period)	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	191		
Units: Percent change				
arithmetic mean (standard deviation)	-90.6 (± 11.3)	-91.7 (± 9.9)		

Statistical analyses

Statistical analysis title	Percent change from Baseline in PASI at Week 16
Comparison groups	MSB11022 (Core Treatment Period) v EU-Humira
Number of subjects included in analysis	394
Analysis specification	Pre-specified
Analysis type	equivalence[2]
Parameter estimate	Least Square (LS) Mean difference
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.21
upper limit	2.98

Notes:

[2] - MSB11022 was considered equivalent to EU-Humira if the 95% CI for the treatment difference was included in the equivalence interval [-15%, 15%]).

Secondary: Percentage of Subjects Who Achieved PASI 50, 90 and 100 at Week 16

End point title	Percentage of Subjects Who Achieved PASI 50, 90 and 100 at Week 16

End point description:

PASI correlates to the physician's assessment of psoriasis symptoms including redness of lesions, thickness of lesions, scaliness of lesions and extent of disease. Each parameter is graded from 0-4, 0 refers to no disease and 4 to severe involvement. The body is divided into 4 areas for scoring (head, arms, trunk to groin, legs to top of buttocks), and the final score ranges from 0-72 with higher scores reflecting more disease severity. The PASI 50, 90 and 100 response rate at Week 16 is measured as the percentage of subjects who achieved at least 50, 90 and 100% improvement from baseline PASI score at Week 16. PP analysis set was used.

End point type	Secondary

End point timeframe:

Week 16

End point values	MSB11022 (Core Treatment Period)	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	191		
Units: Percentage of Subjects				
number (not applicable)				
PASI 50	100.0	100.0		

PASI 90	64.0	66.0		
PASI 100	33.0	37.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieved PASI 50, 75, 90 and 100 at Week 24

End point title	Percentage of Subjects Who Achieved PASI 50, 75, 90 and 100 at Week 24

End point description:

PASI correlates to the physician's assessment of psoriasis symptoms including redness of lesions, thickness of lesions, scaliness of lesions and extent of disease. Each parameter is graded from 0-4, 0 refers to no disease and 4 to severe involvement. The body is divided into 4 areas for scoring (head, arms, trunk to groin, legs to top of buttocks), and the final score ranges from 0-72 with higher scores reflecting more disease severity. The PASI 75 response rate at Week 24 is measured as the percentage of subjects who achieved at least 50, 75, 90 and 100% improvement from baseline PASI at Week 24. The ETP-PP Analysis Set included subjects who were in PP Analysis Set & were re-randomized & received treatment in Extended Treatment Period. Here "Number of subjects analyzed" signifies those who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 24

End point values	MSB11022 (Extended Treatment Period)	EU-Humira/EU-Humira	EU-Humira/MSB11022	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	200	94	92	
Units: Percentage of Subjects				
number (not applicable)				
PASI 50	100.0	98.9	100.0	
PASI 75	92.5	88.3	94.6	
PASI 90	74.0	78.7	80.4	
PASI 100	42.5	37.2	35.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieved PASI 50, 75, 90 and 100 at Week 52

End point title	Percentage of Subjects Who Achieved PASI 50, 75, 90 and 100 at Week 52

End point description:

PASI correlates to the physician's assessment of psoriasis symptoms including redness of lesions, thickness of lesions, scaliness of lesions and extent of disease. Each parameter is graded from 0-4, 0 refers to no disease and 4 to severe involvement. The body is divided into 4 areas for scoring (head, arms, trunk to groin, legs to top of buttocks), and the final score ranges from 0-72 with higher scores reflecting more disease severity. The PASI 90 response rate at Week 52 is measured as the percentage of subjects who achieved at least 50, 75, 90 and 100% improvement from baseline PASI at Week 52. The ETP-PP Analysis Set was used. Here "Number of subjects analyzed" signifies those who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 52

End point values	MSB11022 (Extended Treatment Period)	EU-Humira/EU-Humira	EU-Humira/MSB11022	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	186	85	87	
Units: Percentage of Subjects				
number (not applicable)				
PASI 50	97.8	100.0	100.0	
PASI 75	90.9	92.9	93.1	
PASI 90	76.3	78.8	85.1	
PASI 100	53.8	54.1	57.5	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in PASI at Week 24 and 52

End point title	Percent Change From Baseline in PASI at Week 24 and 52

End point description:

PASI correlates to the physician's assessment of psoriasis symptoms including redness of lesions, thickness of lesions, scaliness of lesions and extent of disease. Each parameter is graded from 0-4, 0 refers to no disease and 4 to severe involvement. The body is divided into 4 areas for scoring (head, arms, trunk to groin, legs to top of buttocks), and the final score ranges from 0-72, with higher scores reflecting more disease severity. The ETP-PP analysis set was used. Here "n" Signifies those subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline (Extended Treatment Period), Weeks 24 and 52

End point values	MSB11022 (Extended Treatment Period)	EU-Humira/EU-Humira	EU-Humira/MSB11022	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	203	95	96	
Units: Percent change				
geometric mean (standard deviation)				
Week 24 (n= 200, 94, 92)	-92.9 (± 9.9)	-91.3 (± 12.7)	-94.2 (± 8.2)	
Week 52 (n= 186, 85, 87)	-92.8 (± 13.6)	-93.9 (± 9.6)	-94.8 (± 9.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Change from Baseline in Physician's Global Assessment (PGA) Score to "Clear" or "Almost Clear" at Week 16

End point title	Number of Subjects With Change from Baseline in Physician's Global Assessment (PGA) Score to "Clear" or "Almost Clear" at Week 16

End point description:

PGA was assessed relative to baseline condition based on a scale ranged from 0 to 4, where 0 indicates Clear condition (no signs of psoriasis, post-inflammatory hyperpigmentation may be present), 1 indicates Almost clear condition (normal to pink coloration of lesion, no thickening and no to minimal [focal] scaling), 2 indicates Mild condition (pink to light red coloration, just detectable to mild thickening and predominantly fine scaling), 3 indicates Moderate condition (dull bright red, clearly distinguishable erythema, clearly distinguishable to moderate thickening and moderate scaling), and 4 indicates Severe condition (bright to deep dark red coloration, severe thickening with hard edges and severe/coarse scaling covering almost all or all lesions). PP Analysis set was used. Number of subjects with PGA response of Clear or Almost clear at Week 16 were presented.

End point type	Secondary

End point timeframe:

Baseline (Core Treatment Period), Week 16

End point values	MSB11022 (Core Treatment Period)	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	191		
Units: Subjects				
number (not applicable)				
Baseline: Moderate; Week 16: Clear	52	51		
Baseline: Moderate; Week 16: Almost clear	76	59		
Baseline: Severe; Week 16: Clear	16	20		
Baseline: Severe; Week 16: Almost clear	27	26		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Change from Baseline in Physician's Global Assessment (PGA) Score to "Clear" or "Almost Clear" at Week 24 and 52

End point title	Number of Subjects With Change from Baseline in Physician's Global Assessment (PGA) Score to "Clear" or "Almost Clear" at Week 24 and 52

End point description:

PGA was assessed relative to baseline condition based on a scale ranged from 0 to 4, where 0 indicates clear condition (no signs of psoriasis, post-inflammatory hyperpigmentation may be present), 1 indicates Almost clear condition (normal to pink coloration of lesion, no thickening and no to minimal [focal] scaling), 2 indicates mild condition (pink to light red coloration, just detectable to mild thickening and predominantly fine scaling), 3 indicates moderate condition (dull bright red, clearly distinguishable erythema, clearly distinguishable to moderate thickening and moderate scaling), and 4 indicates severe condition (bright to deep dark red coloration, severe thickening with hard edges and severe/coarse scaling covering almost all or all lesions). ETP-PP Analysis set was used. Here "n" indicates number of subjects who we evaluable for this endpoint at specified category. Number of subjects with PGA response of Clear or Almost clear at Week 16 were presented.

End point type	Secondary

End point timeframe:

Baseline (Extended Treatment Period), Week 24 and 52

End point values	MSB11022 (Extended Treatment Period)	EU-Humira/EU-Humira	EU-Humira/MSB11022	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	203	95	96	
Units: Subjects				
number (not applicable)				
Baseline: Moderate; Week 24: Clear (n= 200,94,92)	69	25	25	
Baseline:Moderate;Week 24:AlmostClear(n=200,94,92)	52	24	31	
Baseline: Severe; Week 24: Clear (n= 200,94,92)	18	11	9	
Baseline:Severe; Week 24:Almost Clear(n=200,94,92)	27	14	13	
Baseline: Moderate; Week 52: Clear (n=188,85,87)	74	29	34	
Baseline:Moderate;Week 52:AlmostClear(n=188,85,87)	40	13	16	
Baseline: Severe; Week 52: Clear (n=188,85,87)	29	17	16	
Baseline:Severe; Week 52:Almost Clear(n=188,85,87)	15	6	6	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to achieve PASI 50

End point title	Time to achieve PASI 50

End point description:

PASI correlates to the physician's assessment of psoriasis symptoms including redness of lesions, thickness of lesions, scaliness of lesions and extent of disease. Each parameter is graded from 0-4, 0 refers to no disease and 4 to severe involvement. The body is divided into 4 areas for scoring (head, arms, trunk to groin, legs to top of buttocks), and the final score ranges from 0-72, with higher scores reflecting more disease severity. Time to achieve at least 50% improvement in PASI from baseline was measured. PP analysis set was used.

End point type	Secondary

End point timeframe:

Baseline (Core Treatment Period) up to Month 4

End point values	MSB11022 (Core Treatment Period)	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	191		
Units: Months				
median (full range (min-max))	1.6 (0.2 to 3.7)	1.6 (0.2 to 3.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to achieve PASI 75

End point title	Time to achieve PASI 75

End point description:

PASI correlates to the physician's assessment of psoriasis symptoms including redness of lesions, thickness of lesions, scaliness of lesions and extent of disease. Each parameter is graded from 0-4, 0 refers to no disease and 4 to severe involvement. The body is divided into 4 areas for scoring (head, arms, trunk to groin, legs to top of buttocks), and the final score ranges from 0-72, with higher scores reflecting more disease severity. Time to achieve at least 75% improvement in PASI from baseline was measured. PP analysis set was used.

End point type	Secondary

End point timeframe:

Baseline (Core Treatment Period) up to Month 4

End point values	MSB11022 (Core Treatment Period)	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	191		
Units: Months				
median (full range (min-max))	2.5 (0.2 to 3.5)	1.7 (0.7 to 3.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to achieve PASI 90

End point title	Time to achieve PASI 90

End point description:

PASI correlates to the physician's assessment of psoriasis symptoms including redness of lesions, thickness of lesions, scaliness of lesions and extent of disease. Each parameter is graded from 0-4, 0 refers to no disease and 4 to severe involvement. The body is divided into 4 areas for scoring (head, arms, trunk to groin, legs to top of buttocks), and the final score ranges from 0-72, with higher scores reflecting more disease severity. Time to achieve at least 90% improvement in PASI from baseline was measured. PP analysis set was used.

End point type	Secondary

End point timeframe:

Baseline (Core Treatment Period) up to Month 4

End point values	MSB11022 (Core Treatment Period)	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	191		
Units: Months				
median (full range (min-max))	3.4 (0.7 to 3.5)	2.6 (1.4 to 3.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to achieve PASI 100

End point title	Time to achieve PASI 100

End point description:

PASI correlates to the physician's assessment of psoriasis symptoms including redness of lesions, thickness of lesions, scaliness of lesions and extent of disease. Each parameter is graded from 0-4, 0 refers to no disease and 4 to severe involvement. The body is divided into 4 areas for scoring (head, arms, trunk to groin, legs to top of buttocks), and the final score ranges from 0-72, with higher scores reflecting more disease severity. Time to achieve at least 100% improvement in PASI from baseline was measured. PP analysis set was used.

End point type	Secondary

End point timeframe:

Baseline (Core Treatment Period) up to Month 13.5

End point values	MSB11022 (Overall Treatment Period)	EU-Humira/EU-Humira (Overall Treatment Period)	EU-Humira/MSB11022 (Overall Treatment Period)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	203	95	96	
Units: Month				
median (full range (min-max))	7.2 (0.7 to 11.8)	7.2 (1.6 to 11.8)	8.9 (1.6 to 11.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Clinically Meaningful Differences in Laboratory Values

End point title	Number of Subjects with Clinically Meaningful Differences in Laboratory Values

End point description:

Based on categories of low, normal, or high according to the laboratory normal ranges, there were no clinically meaningful differences across the treatment groups in the numbers of subjects with shifts in Laboratory parameters including hematology, chemistry and urinalysis from normal at Core Baseline to either low or high during the overall treatment period. Clinical meaningful was determined by the investigator. Safety Analysis Set (SAF) included all randomized subjects who received at least 1 dose of MSB11022 or EU-approved Humira in the Core Treatment Period, up to Week 16. Subjects in the Safety Analysis Set were analyzed according to the actual treatment received initially during the relevant treatment period. The ETP-SAF was all re-randomized subjects who received at least 1 dose of MSB11022 or EU-approved Humira in the Extended Treatment Period.

End point type	Secondary

End point timeframe:

Baseline (Core Treatment Period) up to 16; Baseline (Extended Treatment Period) up to Week 54

End point values	MSB11022 (Core Treatment Period)	MSB11022 (Extended Treatment Period)	EU-Humira	EU-Humira/EU-Humira
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	222	213	221	101
Units: Subjects				
Laboratory Values	0	0	0	0

End point values	EU-Humira/MSB11022			

Subject group type	Reporting group			
Number of subjects analysed	101			
Units: Subjects				
Laboratory Values	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Clinically Meaningful Differences in Vital Signs

End point title	Number of Subjects with Clinically Meaningful Differences in Vital Signs

End point description:

Number of subjects with clinically meaningful abnormalities in vital signs were reported. Clinical meaningful was determined by the investigator. Safety analysis set was used for Core Treatment Period. ETP-SAF was used for Extended Treatment Period.

End point type	Secondary

End point timeframe:

Baseline (Core Treatment Period) up to 16; Baseline (Extended Treatment Period) up to Week 54

End point values	MSB11022 (Core Treatment Period)	MSB11022 (Extended Treatment Period)	EU-Humira	EU-Humira/EU-Humira
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	222	213	221	101
Units: Subjects				
Vital signs	0	0	0	0

End point values	EU-Humira/MSB11022			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: Subjects				
Vital signs	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Clinically Significant Abnormalities in 12-Electrocardiogram (12-ECG)

End point title	Number of Subjects with Clinically Significant Abnormalities in

	12-Electrocardiogram (12-ECG)

End point description:

Number of subjects with clinically significant abnormalities in 12-ECG were reported. Clinical significance was determined by the investigator. Safety analysis set was used for Core Treatment Period. ETP-SAF was used for Extended Treatment Period.

End point type	Secondary

End point timeframe:

Baseline (Core Treatment Period) up to 16; Baseline (Extended Treatment Period) up to Week 54

End point values	MSB11022 (Core Treatment Period)	MSB11022 (Extended Treatment Period)	EU-Humira	EU-Humira/EU-Humira
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	222	213	221	101
Units: Subjects				
12-ECG	0	1	0	1

End point values	EU-Humira/MSB11022			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: Subjects				
12-ECG	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Serum Concentration at Week 16

End point title	Observed Serum Concentration at Week 16

End point description:

The Pharmacokinetic (PK) Analysis Set included all subjects in the SAF who also had at least 1 measurable post-dose concentration.

End point type	Secondary

End point timeframe:

Week 16

End point values	MSB11022 (Core Treatment Period)	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	192	170		
Units: Nanogram per milliliter (ng/mL)				
geometric mean (standard deviation)	6990 (± 4504)	6410 (± 4152)		

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Serum Concentration at Week 24 and 52

End point title	Observed Serum Concentration at Week 24 and 52

End point description:

The ETP-PK analysis included all subjects in the ETP Safety Analysis Set who had at least 1 measurable post-dose concentration in the Extended Treatment Period, without any important protocol deviations that could have impacted the quality of the PK data during the Extended Treatment Period.

End point type	Secondary

End point timeframe:

Week 24 and 52

End point values	MSB11022 (Extended Treatment Period)	EU-Humira/EU-Humira	EU-Humira/MSB11022	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	198	87	92	
Units: ng/mL				
geometric mean (standard deviation)				
Week 24 (n= 184, 86, 85)	6240 (± 4569)	5870 (± 4516)	6430 (± 4610)	
Week 52 (n= 161, 76, 72)	6910 (± 5750)	5930 (± 4529)	6600 (± 5394)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Change in Physician’s Global Assessment (PGA) From Baseline at Week 16

End point title	Number of Subjects With Change in Physician’s Global Assessment (PGA) From Baseline at Week 16

End point description:

PGA was assessed relative to baseline condition based on a scale ranged from 0 to 4, where 0 indicates clear condition (no signs of psoriasis, post-inflammatory hyperpigmentation may be present), 1 indicates Almost clear condition (normal to pink coloration of lesion, no thickening and no to minimal [focal] scaling), 2 indicates mild condition (pink to light red coloration, just detectable to mild thickening

and predominantly fine scaling), 3 indicates moderate condition (dull bright red, clearly distinguishable erythema, clearly distinguishable to moderate thickening and moderate scaling), and 4 indicates severe condition (bright to deep dark red coloration, severe thickening with hard edges and severe/coarse scaling covering almost all or all lesions). PP Analysis set was used. Only categories for which subjects recorded a PGA response were included below.

End point type	Secondary

End point timeframe:

Baseline (Core Treatment Period), Week 16

End point values	MSB11022 (Core Treatment Period)	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	191		
Units: Subjects				
Baseline- Moderate; Week 16- Clear	52	51		
Baseline- Moderate; Week 16- Almost Clear	76	59		
Baseline- Moderate; Week 16- Mild	16	17		
Baseline- Moderate; Week 16- Moderate	2	1		
Baseline- Severe; Week 16- Clear	16	20		
Baseline- Severe; Week 16- Almost Clear	27	26		
Baseline- Severe; Week 16- Mild	12	16		
Baseline- Severe; Week 16- Moderate	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Change in Physician’s Global Assessment (PGA) From Baseline at Week 24

End point title	Number of Subjects With Change in Physician’s Global Assessment (PGA) From Baseline at Week 24

End point description:

PGA was assessed relative to baseline condition based on a scale ranged from 0 to 4, where 0 indicates clear condition (no signs of psoriasis, post-inflammatory hyperpigmentation may be present), 1 indicates Almost clear condition (normal to pink coloration of lesion, no thickening and no to minimal [focal] scaling), 2 indicates mild condition (pink to light red coloration, just detectable to mild thickening and predominantly fine scaling), 3 indicates moderate condition (dull bright red, clearly distinguishable erythema, clearly distinguishable to moderate thickening and moderate scaling), and 4 indicates severe condition (bright to deep dark red coloration, severe thickening with hard edges and severe/coarse scaling covering almost all or all lesions). ETP-PP Analysis set was used. Only categories for which subjects recorded a PGA response were included
below.

End point type	Secondary

End point timeframe:

Baseline (Extended Treatment Period), Week 24

End point values	MSB11022 (Extended Treatment Period)	EU-Humira/EU-Humira	EU-Humira/MSB11022	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	200	94	92	
Units: Subjects				
Baseline- Moderate; Week 24- Clear	69	25	25	
Baseline- Moderate; Week 24- Almost Clear	52	24	31	
Baseline- Moderate; Week 24- Mild	21	10	7	
Baseline- Moderate; Week 24- Moderate	2	2	0	
Baseline- Severe; Week 24- Clear	18	11	9	
Baseline- Severe; Week 24- Almost Clear	27	14	13	
Baseline- Severe; Week 24- Mild	9	6	6	
Baseline- Severe; Week 24- Moderate	2	1	1	
Baseline- Severe; Week 24- Severe	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Change in Physician’s Global Assessment (PGA) From Baseline at Week 52

End point title	Number of Subjects With Change in Physician’s Global Assessment (PGA) From Baseline at Week 52

End point description:

PGA was assessed relative to baseline condition based on a scale ranged from 0 to 4, where 0 indicates clear condition (no signs of psoriasis, post-inflammatory hyperpigmentation may be present), 1 indicates Almost clear condition (normal to pink coloration of lesion, no thickening and no to minimal [focal] scaling), 2 indicates mild condition (pink to light red coloration, just detectable to mild thickening and predominantly fine scaling), 3 indicates moderate condition (dull bright red, clearly distinguishable erythema, clearly distinguishable to moderate thickening and moderate scaling), and 4 indicates severe condition (bright to deep dark red coloration, severe thickening with hard edges and severe/coarse scaling covering almost all or all lesions). ETP-PP Analysis set was used. Here "Number of subjects analyzed" signifies those who were evaluable for this endpoint. Only categories for which subjects recorded a PGA response were included below.

End point type	Secondary

End point timeframe:

Baseline (Extended Treatment Period), Week 52

End point values	MSB11022 (Extended Treatment Period)	EU-Humira/EU-Humira	EU-Humira/MSB11022	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	188	85	87	
Units: Subjects				
Baseline- Moderate; Week 52- Clear	74	29	34	
Baseline- Moderate; Week 52- Almost Clear	40	13	16	
Baseline- Moderate; Week 52- Mild	17	11	6	
Baseline- Moderate; Week 52- Moderate	4	0	4	
Baseline- Moderate; Week 52- Missing	1	0	0	
Baseline- Severe; Week 52- Clear	29	17	16	
Baseline- Severe; Week 52- Almost Clear	15	6	6	
Baseline- Severe; Week 52- Mild	3	7	3	
Baseline- Severe; Week 52- Moderate	3	2	2	
Baseline- Severe; Week 52- Severe	1	0	0	
Baseline- Severe; Week 52- Missing	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Dermatology Life Quality Index (DLQI) at Week 16

End point title	Dermatology Life Quality Index (DLQI) at Week 16

End point description:

The DLQI is a 10-item validated quality-of-life questionnaire that covers 6 domains: symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment. The DLQI measures how much subject's skin problems has affected his life. Responses range from 0=Not at all to 3=Very much. The DLQI total score is the sum of individual 10 items and could range from 0 to 30 (higher score indicated
greater negative impact on life). PP analysis set was used. Here "Number of subjects analysed" signifies those who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Weeks 16

End point values	MSB11022 (Core Treatment Period)	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	191		
Units: Units on a scale				
arithmetic mean (standard deviation)	2.4 (± 3.2)	2.5 (± 3.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Dermatology Life Quality Index (DLQI) at Week 24 and 52

End point title	Dermatology Life Quality Index (DLQI) at Week 24 and 52

End point description:

The DLQI is a 10-item validated quality-of-life questionnaire that covers 6 domains: symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment. The DLQI measures how much subject's skin problems has affected his life. Responses range from 0=Not at all to 3=Very much. The DLQI total score is the sum of individual 10 items and could range from 0 to 30 (higher score indicated
greater negative impact on life). ETP-PP analysis set was used. Here "Number of subjects analysed" signifies those who ere evaluable for this endpoint and "n" signifies number of subjects who were evaluable for this endpoint at specified category.

End point type	Secondary

End point timeframe:

Week 24 and 52

End point values	MSB11022 (Extended Treatment Period)	EU-Humira/EU-Humira	EU-Humira/MSB11022	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	203	95	96	
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 24 (n= 200, 94, 92)	2.5 (± 4.1)	2.3 (± 4.0)	2.3 (± 3.9)	
Week 52 (n= 186, 85, 86)	3.0 (± 4.7)	2.1 (± 3.5)	2.7 (± 4.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: European Quality of Life 5-Dimensions and 5-Levels Questionnaire (EQ5D-5L) Descriptive Score at Week 16

End point title	European Quality of Life 5-Dimensions and 5-Levels Questionnaire (EQ5D-5L) Descriptive Score at Week 16

End point description:

The EQ-5D-5L questionnaire assesses 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 5 response options (no problems, slight problems, moderate problems, severe problems and extreme problems) that reflect increasing levels of difficulty. The subject was asked to indicate his/her current health state by selecting the most appropriate level in each of the 5
dimensions. The responses are converted into a single index value, with scores ranging from -0.594 to 1 (a higher score indicates better health state). PP analysis set was used. Here "Number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 16

End point values	MSB11022 (Core Treatment Period)	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	179		
Units: Units on a scale				
arithmetic mean (standard deviation)	0.9 (± 0.1)	0.9 (± 0.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: European Quality of Life 5-Dimensions and 5-Levels Questionnaire (EQ5D-5L) Descriptive Score at Week 24 and 52

End point title	European Quality of Life 5-Dimensions and 5-Levels Questionnaire (EQ5D-5L) Descriptive Score at Week 24 and 52

End point description:

The EQ-5D-5L questionnaire assesses 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 5 response options (no problems, slight problems, moderate problems, severe problems and extreme problems) that reflect increasing levels of difficulty. The subject was asked to indicate his/her current health state by selecting the most appropriate level in each of the 5 dimensions. The responses are converted into a single index value, with scores ranging from -0.594 to 1 (a higher score indicates better health state). ETP-PP analysis set was used. 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 category.

End point type	Secondary

End point timeframe:

Week 24 and 52

End point values	MSB11022 (Extended Treatment Period)	EU-Humira/EU-Humira	EU-Humira/MSB11022	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	203	95	96	
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 24 (n= 200, 94, 92)	0.8 (± 0.1)	0.9 (± 0.1)	0.9 (± 0.1)	
Week 52 (n= 186, 85, 86)	0.9 (± 0.1)	0.9 (± 0.1)	0.8 (± 0.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Health Assessment Questionnaire Disability Index (HAQ-DI) at Week 16

End point title	Health Assessment Questionnaire Disability Index (HAQ-DI) at Week 16

End point description:

HAQ-DI: subject-reported assessment of ability to perform tasks in 8 categories of daily living activities: dress/groom; arise; eat; walk; reach; grip; hygiene; and common activities over past week. Each item scored on 4-point scale from 0 to 3: 0=no difficulty; 1=some difficulty; 2=much difficulty; 3=unable to do. Overall score was computed as the sum of domain scores and divided by the number of domains answered.
Total possible score range 0-3 where 0 = least difficulty and 3 = extreme difficulty. PP analysis set was used. Here "Number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 16

End point values	MSB11022 (Core Treatment Period)	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: Units on a scale				
arithmetic mean (standard deviation)	0.3 (± 0.4)	0.3 (± 0.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Health Assessment Questionnaire Disability Index (HAQ-DI) at Week 24, and 52

End point title	Health Assessment Questionnaire Disability Index (HAQ-DI) at Week 24, and 52

End point description:

HAQ-DI: subject-reported assessment of ability to perform tasks in 8 categories of daily living activities: dress/groom; arise; eat; walk; reach; grip; hygiene; and common activities over past week. Each item scored on 4-point scale from 0 to 3: 0=no difficulty; 1=some difficulty; 2=much difficulty; 3=unable to do. Overall score was computed as the sum of domain scores and divided by the number of domains answered.
Total possible score range 0-3 where 0 = least difficulty and 3 = extreme difficulty. ETP-PP analysis set was used. Here "n" signifies those subjects who were evaluable for this endpoint at specified category.

End point type	Secondary

End point timeframe:

Week 24 and 52

End point values	MSB11022 (Extended Treatment Period)	EU-Humira/EU-Humira	EU-Humira/MSB11022	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	203	95	96	
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 24 (n= 18, 8, 10)	0.3 (± 0.4)	0.2 (± 0.5)	0.4 (± 0.3)	
Week 52 (n= 18, 7, 10)	0.3 (± 0.4)	0.1 (± 0.2)	0.5 (± 0.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Global Assessment for Joints on Visual Analog Scale (PJA-VAS) at Week 16

End point title	Patient Global Assessment for Joints on Visual Analog Scale (PJA-VAS) at Week 16

End point description:

Patient global assessment for joints was measured on a 100 millimeter (mm) VAS scale, where 0 = no pain and 100 = worst possible pain. PP analysis set was used. Here "Number of subjects analyzed" signifies subjects who were evaluable for this endpoint at specified category.

End point type	Secondary

End point timeframe:

Week 16

End point values	MSB11022 (Core Treatment Period)	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: millimeter (mm)				
arithmetic mean (standard deviation)	26.9 (± 28.3)	24.6 (± 24.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Global Assessment for Joints on Visual Analog Scale (PJA-VAS) at Week 24 and 52

End point title	Patient Global Assessment for Joints on Visual Analog Scale (PJA-VAS) at Week 24 and 52

End point description:

Patient global assessment for joints was measured on a 100 millimeter (mm) VAS scale, where 0 = no pain and 100 = worst possible pain. ETP-PP analysis set was used. Here "n" signifies subjects who were evaluable for this endpoint at specified category.

End point type	Secondary
End point timeframe: Week 24 and 52	

End point values	MSB11022 (Extended Treatment Period)	EU-Humira/EU-Humira	EU-Humira/MSB11022	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	203	95	96	
Units: mm				
arithmetic mean (standard deviation)				
Week 24 (n= 18, 8, 10)	29.7 (± 25.3)	20.6 (± 27.1)	24.9 (± 20.5)	
Week 52 (n= 18, 7, 10)	25.0 (± 20.3)	14.7 (± 16.5)	29.5 (± 19.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Anti-Drug Antibodies (ADAs) and Neutralizing Antibodies (NAbs) to Adalimumab at Week 16

End point title	Number of Subjects With Anti-Drug Antibodies (ADAs) and Neutralizing Antibodies (NAbs) to Adalimumab at Week 16
End point description: Number of Subjects With treatment emergent Anti-Drug Antibodies (ADAs) and Neutralizing Antibodies (NAbs) to Adalimumab were reported from baseline to week 16. SAF analysis set was used. Here "Number of subjects analyzed" signifies those who were evaluable for this endpoint.	
End point type	Secondary
End point timeframe: Baseline (Core Treatment Period) up to Week 16	

End point values	MSB11022 (Core Treatment Period)	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	202		
Units: Subjects				
number (not applicable)				
Subjects with ADAs (n= 213, 202)	186	179		
Subjects with Neutralizing Abs (n= 186, 179)	70	70		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Anti-Drug Antibodies (ADAs) and Neutralizing Antibodies (NAbs) to Adalimumab at Week 24, 32, 40 and 52

End point title	Number of Subjects With Anti-Drug Antibodies (ADAs) and Neutralizing Antibodies (NAbs) to Adalimumab at Week 24, 32, 40 and 52

End point description:

Number of Subjects With positive treatment emergent Anti-Drug Antibodies (ADAs) and positive Neutralizing Antibodies (NAbs) to Adalimumab were reported. ETP-SAF analysis set was used. Here "Number of subjects analyzed" signifies those subjects who were evaluable for this endpoint and "n" signifies subjects who were evaluable for this endpoint at specified category.

End point type	Secondary

End point timeframe:

Baseline (Extended Treatment Period), Week 24, 32, 40 and 52

End point values	MSB11022 (Extended Treatment Period)	EU-Humira/EU-Humira	EU-Humira/MSB11022	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	213	101	101	
Units: Subjects				
number (not applicable)				
Week 24: ADAs (n= 208, 96, 97)	185	89	90	
Week 32: ADAs (n= 200, 90, 96)	170	78	85	
Week 40: ADAs (n= 197, 89, 92)	161	72	80	
Week 52: ADAs (n= 194, 87, 87)	162	68	77	
Week 24: NAb (n= 185, 89, 90)	78	42	39	
Week 32: NAb (n= 170, 78, 85)	67	30	32	
Week 40: NAb (n= 160, 72, 80)	70	29	28	
Week 52: NAb (n= 162, 68, 77)	63	29	30	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Drug Antibodies (ADAs) Titers for Adalimumab at Week 16

End point title	Anti-Drug Antibodies (ADAs) Titers for Adalimumab at Week 16

End point description:

Anti-Drug Antibodies (ADAs) Titers for adalimumab up to week 16 was reported. SAF analysis set was used.

End point type	Secondary

End point timeframe:

Baseline (Core Treatment Period) up to Week 16

End point values	MSB11022 (Core Treatment Period)	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	222	221		
Units: Titers				
median (full range (min-max))	8.0 (1 to 2048)	8.0 (1 to 1024)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Drug Antibodies (ADAs) Titers for Adalimumab at Week 24, 32, 40 and 52

End point title	Anti-Drug Antibodies (ADAs) Titers for Adalimumab at Week 24, 32, 40 and 52

End point description:

Anti-Drug Antibodies (ADAs) Titers for adalimumab up at Week 24, 32, 40 and 50 was reported. ETP-SAF analysis set was used.

End point type	Secondary

End point timeframe:

Baseline (Extended Treatment Period), Week 24, 32, 40 and 52

End point values	MSB11022 (Extended Treatment Period)	EU-Humira/EU-Humira	EU-Humira/MSB11022	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	213	101	101	
Units: Titers				
median (full range (min-max))				
Week 24 (n= 185, 89, 90)	16.0 (1 to 4096)	16.0 (1 to 4096)	16.0 (1 to 4096)	
Week 32 (n= 170, 78, 85)	16.0 (1 to 1024)	16.0 (1 to 8192)	16.0 (1 to 16384)	
Week 40 (n= 161, 72, 80)	16.0 (1 to 8192)	16.0 (1 to 8192)	16.0 (1 to 16384)	
Week 52 (n= 162, 68, 77)	8.0 (1 to 4096)	16.0 (1 to 4096)	8.0 (1 to 4096)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Anti-nuclear Antibodies (ANA) and Anti-double-stranded Deoxyribonuclic Acid (Anti-dsDNA) Assessments at week 16

End point title	Number of Subjects with Anti-nuclear Antibodies (ANA) and

	Anti-double-stranded Deoxyribonuclic Acid (Anti-dsDNA) Assessments at week 16

End point description:

Number of subjects ANA and anti-ds DNA values were reported. 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. Safety
analysis set was used. Here "Number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline (Core Treatment Period) up to Week 16

End point values	MSB11022 (Core Treatment Period)	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	221	220		
Units: Subjects				
number (not applicable)				
Subjects with Nagative ANA values	205	190		
Subjects with Positive ANA values	6	10		
Subjects with Nagative anti-ds DNA values	201	186		
Subjects with Intermediate anti-ds DNA values	4	5		
Subjects with Positive anti-ds DNA values	4	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Anti-nuclear Antibodies (ANA) and Anti-double-stranded Deoxyribonuclic Acid (Anti-dsDNA) Assessments at Week 24, 32, 40 and 52

End point title	Number of Subjects with Anti-nuclear Antibodies (ANA) and Anti-double-stranded Deoxyribonuclic Acid (Anti-dsDNA) Assessments at Week 24, 32, 40 and 52

End point description:

Number of subjects ANA and anti-ds DNA values were reported. 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. ETP-SAF was used. Here "Number of subjects analyzed" signifies those subjects who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline (Extended Treatment Period), Week 24, 32, 40 and 52

End point values	MSB11022 (Extended Treatment Period)	EU-Humira/EU-Humira	EU-Humira/MSB11022	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	213	101	101	
Units: Subjects				
number (not applicable)				
Week 24: Negative ANA: (n= 201, 94, 97)	188	89	92	
Week 32: Negative ANA: (n= 199, 88, 95)	186	85	88	
Week 40: Negative ANA: (n= 196, 91, 92)	178	85	85	
Week 52: Negative ANA: (n= 193, 87, 87)	185	84	79	
Week 24: Positive ANA: (n= 201, 94, 97)	13	5	5	
Week 32: Positive ANA: (n= 199, 88, 95)	13	3	7	
Week 40: Positive ANA: (n= 196, 91, 92)	18	6	7	
Week 52: Positive ANA: (n= 193, 87, 87)	8	3	8	
Week 24: Negative anti-dsDNA: (n= 202, 95, 94)	191	89	88	
Week 32: Negative anti-dsDNA: (n= 199, 88, 93)	184	83	86	
Week 40: Negative anti-dsDNA: (n= 196, 91, 92)	179	86	84	
Week 52: Negative anti-dsDNA: (n= 192, 87, 88)	173	81	79	
Week 24: Positive anti-dsDNA: (n= 202, 95, 94)	8	3	5	
Week 32: Positive anti-dsDNA: (n= 199, 88, 93)	8	3	5	
Week 40: Positive anti-dsDNA: (n= 196, 91, 92)	10	3	7	
Week 52: Positive anti-dsDNA: (n= 192, 87, 88)	11	2	7	
Week 24: Intermediate anti-dsDNA: (n= 202, 95, 94)	3	3	1	
Week 32: Intermediate anti-dsDNA: (n= 199, 88, 93)	7	2	2	
Week 40: Intermediate anti-dsDNA: (n= 196, 91, 92)	7	2	1	
Week 52: Intermediate anti-dsDNA: (n= 192, 87, 88)	8	4	2	

Statistical analyses

No statistical analyses for this end point

Secondary: European Quality of Life 5-Dimensions and 5-Levels Questionnaire (EQ5D-5L) Based on VAS Score at Week 16

End point title	European Quality of Life 5-Dimensions and 5-Levels Questionnaire (EQ5D-5L) Based on VAS Score at Week 16

End point description:

The EQ-5D-5L questionnaire assesses 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 5 response options (no problems, slight problems, moderate problems, severe problems and extreme problems) that reflect increasing levels of difficulty. The subject was asked to indicate his/her current health state by selecting the most appropriate level on a visual analog scale, where the subject was asked to rate current health status on a scale of 0 to 100, with 0 being the worst imaginable health state. PP analysis set was used. 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 category.

End point type	Secondary

End point timeframe:

Week 16

End point values	MSB11022 (Core Treatment Period)	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	179		
Units: Units on a scale				
arithmetic mean (standard deviation)	81.9 (± 13.9)	83.1 (± 15.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: European Quality of Life 5-Dimensions and 5-Levels Questionnaire (EQ5D-5L) Based on VAS Score at Week 24 and 52

End point title	European Quality of Life 5-Dimensions and 5-Levels Questionnaire (EQ5D-5L) Based on VAS Score at Week 24 and 52

End point description:

The EQ-5D-5L questionnaire assesses 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 5 response options (no problems, slight problems, moderate problems, severe problems and extreme problems) that reflect increasing levels of difficulty. The subject was asked to indicate his/her current health state by selecting the most appropriate level on a visual analog scale, where the subject was asked to rate current health status on a scale of 0 to 100, with 0 being the worst imaginable health state. ETP-PP analysis set was used. 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 category.

End point type	Secondary

End point timeframe:

Week 24 and 52

End point values	MSB11022 (Extended Treatment Period)	EU-Humira/EU-Humira	EU-Humira/MSB11022	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	203	95	96	
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 24 (n= 200, 94, 92)	83.2 (± 14.2)	84.2 (± 13.7)	84.3 (± 13.9)	
Week 52 (n= 186, 85, 86)	83.5 (± 15.5)	85.1 (± 13.2)	82.1 (± 16.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs, TEAEs of Special Interest and TEAEs Leading to Death up to Week 16

End point title	Number of Subjects With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs, TEAEs of Special Interest and TEAEs Leading to Death up to Week 16

End point description:

Adverse event(AE) was defined as any untoward medical occurrence in subject which does not necessarily have causal relationship with treatment. AE was any unfavorable and unintended sign(including abnormal laboratory finding), symptom/disease temporally associated with use of medicinal product, whether/not considered related to medicinal product. 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. TEAEs included both Serious TEAEs and non-serious TEAEs. Safety (SAF) Analysis Set was all randomized subjects who received
at least 1 dose of MSB11022 or EU-Humira. Subjects in SAF were analyzed according to actual treatment received initially during the relevant treatment period.

End point type	Secondary

End point timeframe:

Baseline (Core Treatment Period) up to Week 16

End point values	MSB11022 (Core Treatment Period)	EU-Humira		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	221	220		
Units: Subjects				
number (not applicable)				
Subjects with TEAEs	114	117		
Subjects with Serious TEAEs	8	6		
Subjects with TEAEs of special interest	2	3		
Subjects with TEAEs Leading to Death	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs, TEAEs of Special Interest and TEAEs Leading to Death up to Week 54

End point title	Number of Subjects With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs, TEAEs of Special Interest and TEAEs Leading to Death up to Week 54

End point description:

Adverse event(AE) was defined as any untoward medical occurrence in subject which does not necessarily have causal relationship with treatment. AE was any unfavorable and unintended sign(including abnormal laboratory finding), symptom/disease temporally associated with use of medicinal product, whether/not considered related to medicinal product. 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. TEAEs included both Serious TEAEs and non-serious TEAEs. ETP-SAF Analysis Set was used. Subjects in SAF were analyzed according to actual treatment received initially during the relevant treatment period.

End point type	Secondary

End point timeframe:

Baseline (Extended Treatment Period) up to Week 54

End point values	MSB11022 (Extended Treatment Period)	EU-Humira/EU-Humira	EU-Humira/MSB11022	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	213	101	101	
Units: Subjects				
number (not applicable)				
Subjects with TEAEs	142	65	63	
Subjects with Serious TEAEs	12	3	4	
Subjects with TEAEs of special interest	10	1	4	
Subjects with TEAEs Leading to Death	0	1	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline (Core Treatment Period) up to Week 16; Baseline (Extended Treatment Period) up to Week 54

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	MSB11022 (Core Treatment Period)

Reporting group description:

Subjects received MSB11022 subcutaneously at an initial dose of 80 mg on Day 1 of Week 1 followed by 40 mg every other week starting at Week 2 up to and including Week 14 in Core Treatment Period.

Reporting group title	EU-Humira

Reporting group description:

Subjects received EU-Humira subcutaneously at an initial dose of 80 mg on Day 1 of Week 1 followed by 40 mg every other week starting at Week 2 up to and including Week 14 in Core Treatment Period.

Reporting group title	MSB11022 (Extended Treatment Period)

Reporting group description:

Subjects who had achieved PASI 50 and received MSB11022 during Core Treatment Period continued to receive MSB11022 subcutaneously at dose of 40 mg every other week starting at Week 16 up to and including Week 50 in extended treatment period.

Reporting group title	EU-Humira/EU-Humira

Reporting group description:

Subjects who had achieved PASI 50 and received EU-Humira in Core Treatment Period and continued to receive EU-Humira subcutaneously at dose of 40 mg every other week starting at Week 16 up to and including Week 50 after re-randomization in extended treatment period.

Reporting group title	EU-Humira/MSB11022

Reporting group description:

Subjects who had achieved PASI 50 and received EU-Humira in Core Treatment Period were re-randomized to receive MSB11022 subcutaneously at dose of 40 mg every other week starting at Week 16 up to and including Week 50 in extended treatment period.

Serious adverse events	MSB11022 (Core Treatment Period)	EU-Humira	MSB11022 (Extended Treatment Period)
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 221 (3.62%)	6 / 220 (2.73%)	12 / 213 (5.63%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 221 (0.00%)	1 / 220 (0.45%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 221 (0.45%)	0 / 220 (0.00%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular compression			
subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	1 / 213 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Hernia			
subjects affected / exposed	1 / 221 (0.45%)	0 / 220 (0.00%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	0 / 221 (0.00%)	1 / 220 (0.45%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 221 (0.00%)	1 / 220 (0.45%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test increased			
subjects affected / exposed	0 / 221 (0.00%)	1 / 220 (0.45%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	1 / 213 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			

subjects affected / exposed	1 / 221 (0.45%)	0 / 220 (0.00%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial bones fracture			
subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	1 / 213 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament sprain			
subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	1 / 213 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	1 / 213 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial Fibrillation			
subjects affected / exposed	1 / 221 (0.45%)	0 / 220 (0.00%)	1 / 213 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiomyopathy			
subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	1 / 213 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	1 / 213 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive cardiomyopathy			

subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve incompetence			
subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Brain oedema			
subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haematoma			
subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 221 (0.00%)	1 / 220 (0.45%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Conjunctival cyst			
subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Inguinal hernia			

subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	1 / 213 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	1 / 221 (0.45%)	0 / 220 (0.00%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Erythema multiforme			
subjects affected / exposed	1 / 221 (0.45%)	0 / 220 (0.00%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity vasculitis			
subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	1 / 213 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	1 / 213 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	1 / 213 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	1 / 213 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			

subjects affected / exposed	1 / 221 (0.45%)	0 / 220 (0.00%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis bacterial			
subjects affected / exposed	0 / 221 (0.00%)	1 / 220 (0.45%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonsillar abscess			
subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	1 / 213 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection viral			
subjects affected / exposed	1 / 221 (0.45%)	0 / 220 (0.00%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	1 / 213 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal abscess			
subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	0 / 213 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	EU-Humira/EU-	EU-	

	Humira	Humira/MSB11022	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 101 (2.97%)	4 / 101 (3.96%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular compression			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Hernia			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test increased			

subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament sprain			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial Fibrillation			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	2 / 101 (1.98%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Cardiomyopathy			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive cardiomyopathy			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 101 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Brain oedema			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haematoma			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Eye disorders			
Conjunctival cyst			
subjects affected / exposed	0 / 101 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Erythema multiforme			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity vasculitis			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			

subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 101 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar abscess			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (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	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal abscess			

subjects affected / exposed	0 / 101 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	MSB11022 (Core Treatment Period)	EU-Humira	MSB11022 (Extended Treatment Period)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 221 (13.57%)	34 / 220 (15.45%)	59 / 213 (27.70%)
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	11 / 221 (4.98%)	13 / 220 (5.91%)	9 / 213 (4.23%)
occurrences (all)	18	19	19
Injection site pain			
subjects affected / exposed	11 / 221 (4.98%)	11 / 220 (5.00%)	12 / 213 (5.63%)
occurrences (all)	52	28	54
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	11 / 213 (5.16%)
occurrences (all)	0	0	12
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	13 / 221 (5.88%)	15 / 220 (6.82%)	31 / 213 (14.55%)
occurrences (all)	13	16	36
Upper respiratory tract infection			
subjects affected / exposed	0 / 221 (0.00%)	0 / 220 (0.00%)	11 / 213 (5.16%)
occurrences (all)	0	0	15

Non-serious adverse events	EU-Humira/EU-Humira	EU-Humira/MSB11022	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 101 (31.68%)	25 / 101 (24.75%)	
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	5 / 101 (4.95%)	6 / 101 (5.94%)	
occurrences (all)	25	31	

Injection site pain			
subjects affected / exposed	4 / 101 (3.96%)	5 / 101 (4.95%)	
occurrences (all)	4	18	
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	10 / 101 (9.90%)	3 / 101 (2.97%)	
occurrences (all)	11	3	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	12 / 101 (11.88%)	16 / 101 (15.84%)	
occurrences (all)	14	16	
Upper respiratory tract infection			
subjects affected / exposed	5 / 101 (4.95%)	4 / 101 (3.96%)	
occurrences (all)	7	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 February 2016	1. Added 4-month Safety Evaluation visit in synopsis section and schedule of assessments section. 2. Specified procedures for subjects who become QuantiFERON®-TB Gold test (QFT) positive at Weeks 24 or 52 3. Added safety monitoring committee in early termination visit section 7.4.1
21 April 2016	1. Added of planned Week 24 analysis. 2. Observation period added following second and third injection, in-line with first injection in overall trial design and plan. 3. Subjects will be excluded if they have a body weight greater than (>) 120 kilogram instead of Body Mass Index greater than or equals to (>=) 30 kilogram per square meter (kg/m^2). 4. Added more detailed time frame in inclusion criteria. 5. Addedof AST >3^ULN as exclusion for LTBI positive subjects. 6. Removed efficacy assessments during the safety follow-up period.
16 September 2016	1. Updated the list of abbreviations. 2. Updated the sample size. 3. Clarified of the PK analysis subgroup. 4. Concomitant medicines and procedures were removed from 4-month safety follow-up visit. 5. Updated the timing of vital sign measurements updated. 6. Clarified the use of immunogenicity blood samples for PK analysis

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported