



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 | v2 |
| This version publication date | 13 July 2019 |
| First version publication date | 25 October 2018 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data setChange of sponsorship |

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 | 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 | 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 standard deviation | 44.5 ± 12.8 | 42.7 ± 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/MSB11 022 | |
|-------------------------------|---|-------------------------|----------------------------|--|
| 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/MSB11 022 | |
|-------------------------------|---|-------------------------|----------------------------|--|
| 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: 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: 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/MSB11 022 | |
|-------------------------------------|---|-------------------------|----------------------------|--|
| 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 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 were 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/MSB11 022 | |
|---|---|-------------------------|----------------------------|--|
| 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: Almost Clear (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: Almost Clear (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 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 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 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/MSB11 022 (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/MSB11 022 | | | |
|-----------------------------|----------------------------|--|--|--|
| 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/MSB11 022 | | | |
|-----------------------------|----------------------------|--|--|--|
| 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/MSB11 022 | | | |
|-----------------------------|----------------------------|--|--|--|
| 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/MSB11 022 | |
|-------------------------------------|---|-------------------------|----------------------------|--|
| 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/MSB11 022 | |
|--|---|-------------------------|----------------------------|--|
| 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/MSB11 022 | |
|--|---|-------------------------|----------------------------|--|
| 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: | |
| <p>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.</p> | |
| 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 were 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/MSB11 022 | |
|--------------------------------------|---|-------------------------|----------------------------|--|
| 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/MSB11 022 | |
|--------------------------------------|---|-------------------------|----------------------------|--|
| 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 (\pm 0.4) | 0.3 (\pm 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/MSB11 022 | |
|--------------------------------------|---|-------------------------|----------------------------|--|
| 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/MSB11 022 | |
|--------------------------------------|---|-------------------------|----------------------------|--|
| 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/MSB11 022 | |
|--------------------------------|---|-------------------------|----------------------------|--|
| 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/MSB11 022 | |
|-------------------------------|---|-------------------------|----------------------------|--|
| 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 Deoxyribonucleic Acid (Anti-dsDNA) Assessments at week 16

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

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 Negative ANA values | 205 | 190 | | |
| Subjects with Positive ANA values | 6 | 10 | | |
| Subjects with Negative 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 Deoxyribonucleic 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 Deoxyribonucleic 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/MSB11 022 | |
|--|---|-------------------------|----------------------------|--|
| 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/MSB11 022 | |
|--------------------------------------|---|-------------------------|----------------------------|--|
| 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/MSB11 022 | |
|---|---|-------------------------|----------------------------|--|
| 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 occurrences (all) | 4 / 101 (3.96%) 4 | 5 / 101 (4.95%) 18 | |
| Skin and subcutaneous tissue disorders Psoriasis subjects affected / exposed occurrences (all) | 10 / 101 (9.90%) 11 | 3 / 101 (2.97%) 3 | |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) | 12 / 101 (11.88%) 14 | 16 / 101 (15.84%) 16 | |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 5 / 101 (4.95%) 7 | 4 / 101 (3.96%) 4 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 26 February 2016 | <ol style="list-style-type: none">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 523. Added safety monitoring committee in early termination visit section 7.4.1 |
| 21 April 2016 | <ol style="list-style-type: none">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/m²).4. Added more detailed time frame in inclusion criteria.5. Added of AST >3[^]ULN as exclusion for LTBI positive subjects.6. Removed efficacy assessments during the safety follow-up period. |
| 16 September 2016 | <ol style="list-style-type: none">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