



Clinical trial results:

A 52 Week Multicenter, Randomized, Double-Blind, Placebo Controlled Study to Evaluate the Efficacy and Safety of Ixekizumab (LY2439821) in bDMARD Naive Patients with Nonradiographic Axial Spondyloarthritis Summary

| | |
|--------------------------|----------------------|
| EudraCT number | 2015-003938-27 |
| Trial protocol | DE RO FI CZ AT PL NL |
| Global end of trial date | 07 May 2019 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 15 March 2020 |
| First version publication date | 15 March 2020 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | I1F-MC-RHBX |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|---------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02757352 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Trial Number: 16180 |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Eli Lilly and Company |
| Sponsor organisation address | Lilly Corporate Center, Indianapolis, IN, United States, 46285 |
| Public contact | Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877CTLilly, |
| Scientific contact | Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559, |

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 | 07 May 2019 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 07 May 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study is to evaluate the safety and efficacy of the study drug known as ixekizumab in biologic disease modifying antirheumatic drug (bDMARD) naïve participants with nonradiographic axial spondyloarthritis (nonrad-axSpA).

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 02 August 2016 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Czech Republic: 44 |
| Country: Number of subjects enrolled | Argentina: 23 |
| Country: Number of subjects enrolled | Romania: 9 |
| Country: Number of subjects enrolled | United States: 28 |
| Country: Number of subjects enrolled | Japan: 16 |
| Country: Number of subjects enrolled | Russian Federation: 27 |
| Country: Number of subjects enrolled | Canada: 6 |
| Country: Number of subjects enrolled | Austria: 3 |
| Country: Number of subjects enrolled | Korea, Republic of: 22 |
| Country: Number of subjects enrolled | Netherlands: 1 |
| Country: Number of subjects enrolled | Finland: 10 |
| Country: Number of subjects enrolled | Brazil: 3 |
| Country: Number of subjects enrolled | Poland: 57 |
| Country: Number of subjects enrolled | Mexico: 42 |
| Country: Number of subjects enrolled | Germany: 11 |
| Worldwide total number of subjects | 302 |
| EEA total number of subjects | 135 |

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) | 296 |
| From 65 to 84 years | 6 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

This study has 3 periods: Period 1 - Screening; Period 2 - A Double-Blind Treatment Period (Weeks 0 Up to 52); (Inadequate Responders [IR] Week 16-52) followed by a Follow-Up Period (Up to 24 Weeks after last visit).

Pre-assignment

Screening details:

Participants who completed study were eligible to enroll into a long-term study (Study I1F-MC-RHBY [RHBY]) for up to 2 additional years. Participants that do not enroll into study RHBY will complete the Post-Treatment Follow-Up Period.

Period 1

| | |
|------------------------------|---------------------------------|
| Period 1 title | Double-Blind Period (Week 0-16) |
| 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 | Placebo |

Arm description:

Participants received placebo (PBO) as 2 subcutaneous (SC) injections every two weeks (Q2W) to week 52.

| | |
|--|------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Administered SC

| | |
|------------------|-------------------------------|
| Arm title | Ixekizumab 80 mg Q4W (IXEQ4W) |
|------------------|-------------------------------|

Arm description:

Participants received a starting dose of 80 or 160 milligram (mg) of ixekizumab given subcutaneously (SC) at week 0 followed by 80 mg ixekizumab given SC every four weeks (Q4W) to week 52.

| | |
|--|------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Ixekizumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants received a starting dose of 80 or 160 milligram (mg) of ixekizumab given subcutaneously (SC) at week 0 followed by 80 mg ixekizumab given SC every four weeks (Q4W) to week 52.

| | |
|------------------|-------------------------------|
| Arm title | Ixekizumab 80 mg Q2W (IXEQ2W) |
|------------------|-------------------------------|

Arm description:

Participants received a starting dose of 80 or 160 mg of ixekizumab given SC at week 0 followed by 80 mg ixekizumab given SC every two weeks (Q2W) to week 52.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|------------------|
| Investigational medicinal product name | Ixekizumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants received a starting dose of 80 or 160 mg of ixekizumab given SC at week 0 followed by 80 mg ixekizumab given SC (Q2W) to week 52.

| Number of subjects in period 1 | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) |
|--|---------|-------------------------------|-------------------------------|
| Started | 104 | 96 | 102 |
| Received at least one dose of study drug | 104 | 96 | 102 |
| Completed | 97 | 95 | 98 |
| Not completed | 7 | 1 | 4 |
| Consent withdrawn by subject | 5 | 1 | 2 |
| Adverse event, non-fatal | 2 | - | 1 |
| Lost to follow-up | - | - | 1 |

Period 2

| | |
|------------------------------|----------------------------------|
| Period 2 title | Double-Blind Period (Week 16-52) |
| 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 | Placebo |

Arm description:

Participants received placebo as 2 subcutaneous (SC) injections every two weeks (Q2W) to week 52.

| | |
|--|------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Administered SC

| | |
|------------------|-------------------------------|
| Arm title | Ixekizumab 80 mg Q4W (IXEQ4W) |
|------------------|-------------------------------|

Arm description:

Participants received a starting dose of 80 or 160 milligram (mg) of ixekizumab given subcutaneously (SC) at week 0 followed by 80 mg ixekizumab given SC every four weeks (Q4W) to week 52.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|------------------|
| Investigational medicinal product name | Ixekizumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants received a starting dose of 80 or 160 milligram (mg) of ixekizumab given subcutaneously (SC) at week 0 followed by 80 mg ixekizumab given SC every four weeks (Q4W) to week 52.

| | |
|------------------|-------------------------------|
| Arm title | Ixekizumab 80 mg Q2W (IXEQ2W) |
|------------------|-------------------------------|

Arm description:

Participants received a starting dose of 80 or 160 mg of ixekizumab given SC at week 0 followed by 80 mg ixekizumab given SC every two weeks (Q2W) to week 52.

| | |
|--|------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Ixekizumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants received a starting dose of 80 or 160 mg of ixekizumab given SC at week 0 followed by 80 mg ixekizumab given SC (Q2W) to week 52.

| Number of subjects in period 2 | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) |
|--|---------|-------------------------------|-------------------------------|
| Started | 97 | 95 | 98 |
| Completed | 34 | 52 | 52 |
| Not completed | 63 | 43 | 46 |
| Consent withdrawn by subject | 1 | 1 | 4 |
| Adverse event, non-fatal | - | 1 | - |
| Classified as Inadequate Responders (IR) | 62 | 40 | 42 |
| Lack of efficacy | - | 1 | - |

Period 3

| | |
|------------------------------|---|
| Period 3 title | IR Open Label Period (Week 16- Week 52) |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|----|
| Are arms mutually exclusive? | No |
|------------------------------|----|

| | |
|---|--|
| Arm title | PBO Inadequate Responders (IR)/Ixezumab 80 mg Q2W (IXE80Q2W) |
| Arm description: Participants who received placebo in double blind period and were inadequate responders as determined by investigators switched to ixekizumab 80 mg Q2W open label between week 16 to 44. | |
| Arm type | Experimental |
| Investigational medicinal product name | Ixezumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants who received placebo in double blind period and were inadequate responders as determined by investigators switched to ixekizumab 80 mg Q2W open label between week 16 to 44.

| | |
|--|---|
| Arm title | Ixezumab 80 mg Q4W IR (IXE80Q4WIR)/IXE80Q2W |
| Arm description: Participants who received ixekizumab 80 mg Q4W in double blind period and were inadequate responders as determined by investigators switched to ixekizumab 80 mg Q2W open label between week 16 to 44. | |
| Arm type | Experimental |
| Investigational medicinal product name | Ixezumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants who received ixekizumab 80 mg Q4W in double blind period and were inadequate responders as determined by investigators switched to ixekizumab 80 mg Q2W open label between week 16 to 44.

| | |
|---|---------------------|
| Arm title | IXE80Q2WIR/IXE80Q2W |
| Arm description: Participants who received ixekizumab 80 mg Q2W in double blind period and were inadequate responders as determined by investigators continued on the same regimen of ixekizumab 80 mg Q2W open label between week 16 to 44. | |
| Arm type | Experimental |
| Investigational medicinal product name | Ixezumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Participants who received ixekizumab 80 mg Q2W in double blind period and were inadequate responders as determined by investigators continued on the same regimen of ixekizumab 80 mg Q2W open label between week 16 to 44.

| Number of subjects in period 3 | PBO Inadequate Responders (IR)/Ixekezumab 80 mg Q2W | Ixekezumab 80 mg Q4W IR (IXE80Q4WIR)/IXE80Q2W | IXE80Q2WIR/IXE80Q2W |
|---------------------------------|---|---|---------------------|
| Started | 62 | 40 | 42 |
| Initiated Other Biologic Rescue | 2 ^[1] | 0 ^[2] | 3 ^[3] |
| Completed | 55 | 37 | 35 |
| Not completed | 7 | 3 | 7 |
| Consent withdrawn by subject | 2 | 1 | 1 |
| Physician decision | - | - | 1 |
| Adverse event, non-fatal | 3 | - | 1 |
| Pregnancy | - | 1 | - |
| Lack of efficacy | 2 | 1 | 4 |

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Inadequate responders who initiated other biologic rescue were also counted in the not completed row.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Inadequate responders who initiated other biologic rescue were also counted in the not completed row.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Inadequate responders who initiated other biologic rescue were also counted in the not completed row.

Period 4

| | |
|------------------------------|------------------|
| Period 4 title | Follow-Up Period |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo |

Arm description:

Participants discontinued the study early and entered the post-treatment follow-up period. Participants received placebo immediately prior to entering the post-treatment follow-up period.

| | |
|---|----------------------|
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |
| Arm title | Ixekezumab 80 mg Q4W |

Arm description:

Participants discontinued the study early and entered the post-treatment follow-up period. Participants received ixekizumab 80 mg Q4W immediately prior to entering the post-treatment follow-up period.

| | |
|---|----------------------|
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |
| Arm title | Ixekezumab 80 mg Q2W |

Arm description:

Participants discontinued the study early and entered the post-treatment follow-up period. Participants

received ixekizumab 80 mg Q2W immediately prior to entering the post-treatment follow-up period

| | |
|--|--------------------------|
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |
| Arm title | Other Biologic Treatment |
| Arm description: Participants who discontinued study treatment and were on other biologic therapy prior to entering Follow-up period. | |
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |

| Number of subjects in period 4 | Placebo | Ixekizumab 80 mg Q4W | Ixekizumab 80 mg Q2W |
|---------------------------------------|---------|----------------------|----------------------|
| Started | 3 | 5 | 28 |
| Completed | 2 | 4 | 18 |
| Not completed | 1 | 1 | 10 |
| Consent withdrawn by subject | - | 1 | 6 |
| Adverse event, non-fatal | 1 | - | 2 |
| Lost to follow-up | - | - | 1 |
| Withdrawal due to loss of efficacy | - | - | - |
| Lack of efficacy | - | - | 1 |

| Number of subjects in period 4 | Other Biologic Treatment |
|---------------------------------------|--------------------------|
| Started | 5 |
| Completed | 2 |
| Not completed | 3 |
| Consent withdrawn by subject | 2 |
| Adverse event, non-fatal | - |
| Lost to follow-up | - |
| Withdrawal due to loss of efficacy | 1 |
| Lack of efficacy | - |

Baseline characteristics

Reporting groups

| | |
|--|-------------------------------|
| Reporting group title | Placebo |
| Reporting group description: | |
| Participants received placebo (PBO) as 2 subcutaneous (SC) injections every two weeks (Q2W) to week 52. | |
| Reporting group title | Ixekizumab 80 mg Q4W (IXEQ4W) |
| Reporting group description: | |
| Participants received a starting dose of 80 or 160 milligram (mg) of ixekizumab given subcutaneously (SC) at week 0 followed by 80 mg ixekizumab given SC every four weeks (Q4W) to week 52. | |
| Reporting group title | Ixekizumab 80 mg Q2W (IXEQ2W) |
| Reporting group description: | |
| Participants received a starting dose of 80 or 160 mg of ixekizumab given SC at week 0 followed by 80 mg ixekizumab given SC every two weeks (Q2W) to week 52. | |

| Reporting group values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) |
|---|---------|-------------------------------|-------------------------------|
| Number of subjects | 104 | 96 | 102 |
| Age categorical | | | |
| Units: Subjects | | | |
| Age continuous | | | |
| Age | | | |
| Units: years | | | |
| arithmetic mean | 39.9 | 40.9 | 40.0 |
| standard deviation | ± 12.36 | ± 14.47 | ± 12.01 |
| Gender categorical | | | |
| Gender | | | |
| Units: Subjects | | | |
| Female | 61 | 46 | 53 |
| Male | 43 | 50 | 49 |
| Ethnicity (NIH/OMB) | | | |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 25 | 24 | 31 |
| Not Hispanic or Latino | 67 | 57 | 63 |
| Unknown or Not Reported | 12 | 15 | 8 |
| Race (NIH/OMB) | | | |
| Race | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 8 | 2 | 3 |
| Asian | 17 | 13 | 11 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 0 | 0 |
| White | 75 | 80 | 83 |
| More than one race | 3 | 1 | 5 |
| Unknown or Not Reported | 1 | 0 | 0 |
| Region of Enrollment | | | |
| Region of Enrollment | | | |

| | | | |
|-----------------|----|----|----|
| Units: Subjects | | | |
| Argentina | 8 | 6 | 9 |
| Romania | 4 | 1 | 4 |
| United States | 10 | 9 | 9 |
| Czechia | 15 | 16 | 13 |
| Japan | 6 | 5 | 5 |
| Russia | 12 | 7 | 8 |
| Canada | 1 | 3 | 2 |
| Austria | 0 | 1 | 2 |
| South Korea | 9 | 7 | 6 |
| Netherlands | 0 | 0 | 1 |
| Finland | 4 | 3 | 3 |
| Brazil | 0 | 1 | 2 |
| Poland | 19 | 18 | 20 |
| Mexico | 14 | 13 | 15 |
| Germany | 2 | 6 | 3 |

| | | | |
|-------------------------------|-------|--|--|
| Reporting group values | Total | | |
| Number of subjects | 302 | | |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|-----|--|--|
| Age continuous | | | |
| Age | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| Gender | | | |
| Units: Subjects | | | |
| Female | 160 | | |
| Male | 142 | | |
| Ethnicity (NIH/OMB) | | | |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 80 | | |
| Not Hispanic or Latino | 187 | | |
| Unknown or Not Reported | 35 | | |
| Race (NIH/OMB) | | | |
| Race | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 13 | | |
| Asian | 41 | | |
| Native Hawaiian or Other Pacific Islander | 0 | | |
| Black or African American | 0 | | |
| White | 238 | | |
| More than one race | 9 | | |
| Unknown or Not Reported | 1 | | |
| Region of Enrollment | | | |
| Region of Enrollment | | | |

| | | | |
|-----------------|----|--|--|
| Units: Subjects | | | |
| Argentina | 23 | | |
| Romania | 9 | | |
| United States | 28 | | |
| Czechia | 44 | | |
| Japan | 16 | | |
| Russia | 27 | | |
| Canada | 6 | | |
| Austria | 3 | | |
| South Korea | 22 | | |
| Netherlands | 1 | | |
| Finland | 10 | | |
| Brazil | 3 | | |
| Poland | 57 | | |
| Mexico | 42 | | |
| Germany | 11 | | |

End points

End points reporting groups

| | |
|---|--|
| Reporting group title | Placebo |
| Reporting group description: Participants received placebo (PBO) as 2 subcutaneous (SC) injections every two weeks (Q2W) to week 52. | |
| Reporting group title | Ixekizumab 80 mg Q4W (IXEQ4W) |
| Reporting group description: Participants received a starting dose of 80 or 160 milligram (mg) of ixekizumab given subcutaneously (SC) at week 0 followed by 80 mg ixekizumab given SC every four weeks (Q4W) to week 52. | |
| Reporting group title | Ixekizumab 80 mg Q2W (IXEQ2W) |
| Reporting group description: Participants received a starting dose of 80 or 160 mg of ixekizumab given SC at week 0 followed by 80 mg ixekizumab given SC every two weeks (Q2W) to week 52. | |
| Reporting group title | Placebo |
| Reporting group description: Participants received placebo as 2 subcutaneous (SC) injections every two weeks (Q2W) to week 52. | |
| Reporting group title | Ixekizumab 80 mg Q4W (IXEQ4W) |
| Reporting group description: Participants received a starting dose of 80 or 160 milligram (mg) of ixekizumab given subcutaneously (SC) at week 0 followed by 80 mg ixekizumab given SC every four weeks (Q4W) to week 52. | |
| Reporting group title | Ixekizumab 80 mg Q2W (IXEQ2W) |
| Reporting group description: Participants received a starting dose of 80 or 160 mg of ixekizumab given SC at week 0 followed by 80 mg ixekizumab given SC every two weeks (Q2W) to week 52. | |
| Reporting group title | PBO Inadequate Responders (IR)/Ixekizumab 80 mg Q2W (IXE80Q2W) |
| Reporting group description: Participants who received placebo in double blind period and were inadequate responders as determined by investigators switched to ixekizumab 80 mg Q2W open label between week 16 to 44. | |
| Reporting group title | Ixekizumab 80 mg Q4W IR (IXE80Q4WIR)/IXE80Q2W |
| Reporting group description: Participants who received ixekizumab 80 mg Q4W in double blind period and were inadequate responders as determined by investigators switched to ixekizumab 80 mg Q2W open label between week 16 to 44. | |
| Reporting group title | IXE80Q2WIR/IXE80Q2W |
| Reporting group description: Participants who received ixekizumab 80 mg Q2W in double blind period and were inadequate responders as determined by investigators continued on the same regimen of ixekizumab 80 mg Q2W open label between week 16 to 44. | |
| Reporting group title | Placebo |
| Reporting group description: Participants discontinued the study early and entered the post-treatment follow-up period. Participants received placebo immediately prior to entering the post-treatment follow-up period. | |
| Reporting group title | Ixekizumab 80 mg Q4W |
| Reporting group description: Participants discontinued the study early and entered the post-treatment follow-up period. Participants received ixekizumab 80 mg Q4W immediately prior to entering the post-treatment follow-up period. | |
| Reporting group title | Ixekizumab 80 mg Q2W |
| Reporting group description: Participants discontinued the study early and entered the post-treatment follow-up period. Participants received ixekizumab 80 mg Q2W immediately prior to entering the post-treatment follow-up period | |
| Reporting group title | Other Biologic Treatment |

Reporting group description:

Participants who discontinued study treatment and were on other biologic therapy prior to entering Follow-up period.

| | |
|----------------------------|--------------------|
| Subject analysis set title | IXE80Q2W-Q2W |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Participants received a starting dose of 80 ixekizumab as an SC injection at baseline followed by 80 mg of ixekizumab every two weeks (Q2W) week 2 to week 52.

| | |
|----------------------------|--------------------|
| Subject analysis set title | IXE80Q4W-Q4W |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Participants received a starting dose of 80 ixekizumab as an SC injection followed by 80 mg of ixekizumab Q4W week 4 to week 52.

| | |
|----------------------------|--------------------|
| Subject analysis set title | PBO-IXE80Q2W |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Participants who received placebo in double blind period and were inadequate responders switched to ixekizumab 80 mg Q2W open-label between week 16 - 44.

| | |
|----------------------------|--------------------|
| Subject analysis set title | IXE80Q4W-Q2W |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Participants who received ixekizumab 80 mg Q4W in double blind period and were inadequate responders switched to ixekizumab 80 mg Q2W open label between week 16 - 44.

| | |
|----------------------------|---------------------|
| Subject analysis set title | IXEQ2W (80S)/IXEQ2W |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Ixekizumab was administered subcutaneously every 2 weeks with an 80 mg starting dose at week 0. 80 mg subcutaneously (80S)

| | |
|----------------------------|--------------------------------|
| Subject analysis set title | IXEQ2W (80S)/IXEQ2W Open Label |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Ixekizumab was administered every 2 weeks with an 80 mg starting dose at Week 0, then ixekizumab 80 mg Q2W open label between Week 16 and Week 52.

| | |
|----------------------------|----------------------|
| Subject analysis set title | IXEQ2W (160S)/IXEQ2W |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Ixekizumab was administered subcutaneously every 2 weeks with 160 mg starting dose at week 0. 160 mg subcutaneously (160S)

| | |
|----------------------------|---------------------------------|
| Subject analysis set title | IXEQ2W (160s)/IXEQ2W Open Label |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Ixekizumab was administered subcutaneously every 2 weeks with 160 mg starting dose at week 0 then ixekizumab 80 mg Q2W open label between Week 16 and Week 52.

| | |
|----------------------------|---------------------|
| Subject analysis set title | IXEQ4W (80S) IXEQ4W |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Ixekizumab was administered subcutaneously every 4 weeks with an 80 mg starting dose at week 0.

| | |
|----------------------------|--------------------------------|
| Subject analysis set title | IXEQ4W (80S)/IXEQ2W Open Label |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Ixekizumab was administered subcutaneously every 4 weeks with an 80 mg starting dose at week 0 then ixekizumab 80 mg Q2W open label between Week 16 and Week 52.

| | |
|----------------------------|----------------------|
| Subject analysis set title | IXEQ4W (160S)/IXEQ4W |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Ixekizumab was administered subcutaneously every 4 weeks with 160 mg starting dose at week 0.

| | |
|----------------------------|---------------------------------|
| Subject analysis set title | IXEQ4W (160S) IXEQ2W Open Label |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Ixekizumab was administered subcutaneously every 4 weeks with 160 mg starting dose at week 0 then ixekizumab 80 mg Q2W open label between Week 16 and Week 52.

| | |
|----------------------------|-----------------------|
| Subject analysis set title | PBO/IXEQ2W Open Label |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Placebo was administered at week 0 then ixekizumab 80 mg Q2W open label between Week 16 and Week 52.

| | |
|----------------------------|--------------------|
| Subject analysis set title | IXEQ2W(80S) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

PK analysis at Week 16

| | |
|----------------------------|--------------------|
| Subject analysis set title | IXEQ2W(160S) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

PK analysis at Week 16

| | |
|----------------------------|--------------------|
| Subject analysis set title | IXEQ4W(80S) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

PK analysis at Week 16

| | |
|----------------------------|--------------------|
| Subject analysis set title | IXEQ4W(160S) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

PK analysis at Week 16

Primary: Percentage of Participants Achieving an Assessment of Spondyloarthritis International Society 40 (ASAS40) Response

| | |
|-----------------|--|
| End point title | Percentage of Participants Achieving an Assessment of Spondyloarthritis International Society 40 (ASAS40) Response |
|-----------------|--|

End point description:

ASAS40 is defined as a greater than or equal to (\geq)40% improvement and an absolute improvement from baseline of ≥ 2 units (ranges 0 to 10) in at least 3 of the 4 domains (Patient Global, Spinal Pain, Function, and Inflammation), without any worsening in the remaining domain. 1) Patient Global: How active was your spondylitis during the last week? score ranges 0 (not active) to 10 (very active). 2) Spinal Pain: How much spinal pain due to Ankylosing spondylitis? score ranges 0 (no pain) to 10 (severe pain). 3) Bath Ankylosing Spondylitis Functional Index: Participant is asked to rate the difficulty associated with 10 individual basic functional activities. Responses were captured using numeric rating scale (NRS) (ranges 0 to 10) with a higher score of worse function. 4) Inflammation based on mean of Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) question 5 and 6 (mean of intensity, duration of stiffness). Score ranges (0 (non) to 10 (very severe)).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Week 16

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-----------------------------------|--------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 ^[1] | 96 ^[2] | 102 ^[3] | |
| Units: percentage of participants | | | | |
| number (not applicable) | 19.0 | 35.4 | 40.2 | |

Notes:

[1] - Total participants 105. One participant who did not receive study drug is included in the analysis.

[2] - All randomized participants.

[3] - All randomized participants.

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Statistical Analysis ASAS40 |
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[4] |
| P-value | = 0.009 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.36 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.23 |
| upper limit | 4.51 |

Notes:

[4] - Total participants 201. One participant who did not receive study drug was included in the analysis.

| | |
|---|---|
| Statistical analysis title | Statistical Analysis ASAS40 |
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[5] |
| P-value | = 0.002 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.78 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.48 |
| upper limit | 5.25 |

Notes:

[5] - Total participants 207. One participant who did not receive study drug was included in the analysis.

Primary: Percentage of Participants Achieving an ASAS40 Response

| | |
|-----------------|---|
| End point title | Percentage of Participants Achieving an ASAS40 Response |
|-----------------|---|

End point description:

ASAS40 is defined as a greater than or equal to (\geq)40% improvement and an absolute improvement from baseline of ≥ 2 units (ranges 0 to 10) in at least 3 of the 4 domains (Patient Global, Spinal Pain, Function, and Inflammation), without any worsening in the remaining domain. 1) Patient Global: How active was your spondylitis during the last week? score ranges 0 (not active) to 10 (very active). 2) Spinal Pain: How much spinal pain due to Ankylosing spondylitis? score ranges 0 (no pain) to 10 (severe pain). 3) Bath Ankylosing Spondylitis Functional Index: Participant is asked to rate the difficulty associated with 10 individual basic functional activities. Responses were captured using numeric rating scale (NRS) (ranges 0 to 10) with a higher score of worse function. 4) Inflammation based on mean of Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) question 5 and 6 (mean of intensity, duration of stiffness). Score ranges (0 (non) to 10 (very severe)).

| | |
|----------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| Week 52 | |

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-----------------------------------|--------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 ^[6] | 96 ^[7] | 102 ^[8] | |
| Units: percentage of participants | | | | |
| number (not applicable) | 13.3 | 30.2 | 31.4 | |

Notes:

[6] - Total participants 105. One participant who did not receive study drug is included in the analysis.

[7] - All randomized participants.

[8] - All randomized participants.

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Percentage of Participants Achieving ASAS40 |
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[9] |
| P-value | = 0.004 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.82 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.38 |
| upper limit | 5.77 |

Notes:

[9] - Total participants 201. One participant who did not receive study drug was included in the analysis.

| | |
|-----------------------------------|---|
| Statistical analysis title | Percentage of Participants Achieving ASAS40 |
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |

| | |
|---|-----------------------------|
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[10] |
| P-value | = 0.004 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.85 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.4 |
| upper limit | 5.77 |

Notes:

[10] - Total participants 207. One participant who received at least one dose of study drug was included in the analysis.

Secondary: Change from Baseline in Ankylosing Spondylitis Disease Activity Score (ASDAS)

| | |
|-----------------|---|
| End point title | Change from Baseline in Ankylosing Spondylitis Disease Activity Score (ASDAS) |
|-----------------|---|

End point description:

ASDAS is a composite index to assess disease activity in axial spondyloarthritis (axSpA). ASDAS parameters used with (C-reactive protein [CRP] as acute phase reactant) are: 1) Total back pain 2) Patient global 3) Peripheral pain/swelling, duration of morning stiffness 4) CRP in mg/L: ASDAScrp is calculated with the equation: $0.121 \times \text{total back pain} + 0.110 \times \text{patient global} + 0.073 \times \text{peripheral pain/swelling} + 0.058 \times \text{duration of morning stiffness} + 0.579 \times \ln(\text{CRP}+1)$. CRP is in milligram/liter (mg/L), the range of other variables is from 0 to 10. Data from five variables combined to yield a score (0.6361 to no defined upper limit), where higher scores indicated higher disease activity. Ln represents the natural logarithm. Least squares mean (LS Mean) was derived from mixed models repeated measure analysis (MMRM) with treatment, geographic region, screening MRI/CRP status, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Week 16

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-------------------------------------|---------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 ^[11] | 96 ^[12] | 102 ^[13] | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | -0.58 (± 0.095) | -1.12 (± 0.097) | -1.26 (± 0.095) | |

Notes:

[11] - All randomized participants with evaluable data.

[12] - All randomized participants with evaluable data.

[13] - All randomized participants with evaluable data.

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Statistical analysis ASDAS |
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.54 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.81 |
| upper limit | -0.28 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.136 |

| | |
|---|---|
| Statistical analysis title | Statistical analysis ASDAS |
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.68 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.94 |
| upper limit | -0.41 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.134 |

Secondary: Change from Baseline in Ankylosing Spondylitis Disease Activity Score (ASDAS)

| | |
|-----------------|---|
| End point title | Change from Baseline in Ankylosing Spondylitis Disease Activity Score (ASDAS) |
|-----------------|---|

End point description:

ASDAS is a composite index to assess disease activity in axSpA. ASDAS parameters used (with CRP as acute phase reactant) are: 1) Total back pain 2) Patient global 3) Peripheral pain/swelling 4) Duration of morning stiffness 5) CRP in mg/L: ASDAScrp is calculated with the following equation: $0.121 \times \text{total back pain} + 0.110 \times \text{patient global} + 0.073 \times \text{peripheral pain/swelling} + 0.058 \times \text{duration of morning stiffness} + 0.579 \times \ln(\text{CRP}+1)$. CRP is in milligram/liter (mg/L), the range of other variables is from 0 to 10. Data from five variables combined to yield a score (0.6361 to no defined upper limit), where higher scores indicated higher disease activity. Ln represents the natural logarithm. LS Mean was derived from MMRM with treatment, geographic region, screening MRI/CRP status, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 52 | |

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-------------------------------------|---------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 ^[14] | 96 ^[15] | 102 ^[16] | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | -0.78 (± 0.136) | -1.39 (± 0.116) | -1.47 (± 0.116) | |

Notes:

[14] - All randomized participants with evaluable data.

[15] - All randomized participants with evaluable data.

[16] - All randomized participants with evaluable data.

Statistical analyses

| Statistical analysis title | Statistical Analysis ASDAS |
|---|---|
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.61 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.96 |
| upper limit | -0.26 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.179 |

| Statistical analysis title | Statistical Analysis ASDAS |
|---|---|
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.69 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.05 |
| upper limit | -0.34 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.178 |

Secondary: Number of Participants without Clinically Meaningful Changes in Background Therapy

| | |
|--|--|
| End point title | Number of Participants without Clinically Meaningful Changes in Background Therapy |
| End point description: Number of participants without changes in background therapy while on originally randomized treatment. | |
| End point type | Secondary |
| End point timeframe: Baseline, Week 52 | |

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-----------------------------|---------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 ^[17] | 96 ^[18] | 102 ^[19] | |
| Units: participants | | | | |
| number (not applicable) | 98 | 90 | 100 | |

Notes:

[17] - Total participants 105. One participant who did not receive study drug is included in the analysis.

[18] - All randomized participants.

[19] - All randomized participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in 36-Item Short Form Health Survey (SF-36) Physical Component Summary (PCS) Score

| | |
|--|---|
| End point title | Change from Baseline in 36-Item Short Form Health Survey (SF-36) Physical Component Summary (PCS) Score |
| End point description: The SF-36 is a 36-item patient-administered measure designed to be a short, multipurpose assessment of health in the areas of physical functioning, role – physical, role – emotional, bodily pain, vitality, social functioning, mental health, and general health. The Physical Component Summary score ranges from 0 to 100; higher scores indicate better levels of function and/or better health. LS Mean was derived from MMRM with treatment, geographic region, screening MRI/CRP status, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors. | |
| End point type | Secondary |
| End point timeframe: Baseline, Week 16 | |

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-------------------------------------|------------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 ^[20] | 96 ^[21] | 102 ^[22] | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | 5.2103 (\pm 0.7999) | 8.0612 (\pm 0.8129) | 7.9600 (\pm 0.8023) | |

Notes:

[20] - All randomized participants with evaluable data.

[21] - All randomized participants with evaluable data.

[22] - All randomized participants with evaluable data.

Statistical analyses

| Statistical analysis title | Change from Baseline in 36-Item Short Form Health |
|---|---|
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.013 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | 2.8509 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.6092 |
| upper limit | 5.0926 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.139 |

| Statistical analysis title | Change from Baseline in 36-Item Short Form Health |
|---|---|
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.015 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | 2.7497 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.5299 |
| upper limit | 4.9694 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.1278 |

Secondary: Change from Baseline in 36-Item Short Form Health Survey (SF-36) Physical Component Summary (PCS) Score

| | |
|-----------------|---|
| End point title | Change from Baseline in 36-Item Short Form Health Survey (SF-36) Physical Component Summary (PCS) Score |
|-----------------|---|

End point description:

The medical outcomes study 36-item short-form health survey (SF-36) SF-36 PCS are summarized using the t-scores. The summary scores range from 0 to 100, with higher scores indicating better levels of function and/or better health. LS Mean was derived from MMRM with treatment, geographic region, screening MRI/CRP status, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Week 52

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-------------------------------------|------------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 ^[23] | 96 ^[24] | 102 ^[25] | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | 4.7210 (\pm 1.2459) | 8.9211 (\pm 1.0783) | 9.3291 (\pm 1.0810) | |

Notes:

[23] - All randomized participants with evaluable data.

[24] - All randomized participants with evaluable data.

[25] - All randomized participants with evaluable data.

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Change from Baseline in 36-Item Short Form Health |
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.012 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | 4.2001 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.9525 |
| upper limit | 7.4477 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.6467 |

| | |
|---|---|
| Statistical analysis title | Change from Baseline in 36-Item Short Form Health |
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.006 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | 4.6081 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.3629 |
| upper limit | 7.8533 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.6455 |

Secondary: Percentage of Participants Achieving ASDAS Low Disease Activity

| | |
|-----------------|---|
| End point title | Percentage of Participants Achieving ASDAS Low Disease Activity |
|-----------------|---|

End point description:

ASDAS is a composite index to assess disease activity in axSpA. ASDAS low disease activity is defined as a score of <2.1. The parameters used for the ASDAS (with CRP as acute phase reactant) are total back pain, patient global, peripheral pain/swelling, duration of morning stiffness and CRP in mg/L. The ASDAScrp is calculated with the following equation: $0.121 \times \text{total back pain} + 0.110 \times \text{patient global} + 0.073 \times \text{peripheral pain/swelling} + 0.058 \times \text{duration of morning stiffness} + 0.579 \times \ln(\text{CRP} + 1)$. CRP is in mg/liter, the range of other variables is from 0(normal) to 10(very severe); Ln represents the natural logarithm). Data from five variables combined to yield a score (0.6361 to no defined upper limit), where higher the score worse the disease activity.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 16

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-----------------------------------|---------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 ^[26] | 94 ^[27] | 102 ^[28] | |
| Units: percentage of participants | | | | |
| number (not applicable) | 12.4 | 27.7 | 32.4 | |

Notes:

[26] - Total participants 105. One participant who did not receive study drug is included in the analysis.

[27] - All randomized participants with baseline ASDAS <2.1.

[28] - All randomized participants with baseline ASDAS <2.1.

Statistical analyses

| | |
|-----------------------------------|---|
| Statistical analysis title | Statistical Analysis ASDAS Low Disease |
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |

| | |
|---|-----------------------------|
| Number of subjects included in analysis | 198 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[29] |
| P-value | = 0.008 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.73 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.3 |
| upper limit | 5.76 |

Notes:

[29] - Total participants 199. One participant who did not receive study drug is included in the analysis.

| | |
|---|---|
| Statistical analysis title | Statistical Analysis ASDAS Low Disease |
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[30] |
| P-value | < 0.001 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 3.43 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.66 |
| upper limit | 7.08 |

Notes:

[30] - Total participants 207. One participant who did not receive study drug is included in the analysis.

Secondary: Percentage of Participants Achieving ASDAS Low Disease Activity

| | |
|-----------------|---|
| End point title | Percentage of Participants Achieving ASDAS Low Disease Activity |
|-----------------|---|

End point description:

ASDAS is a composite index to assess disease activity in axSpA. ASDAS low disease activity is defined as a score of <2.1. The parameters used for the ASDAS (with CRP as acute phase reactant) are total back pain, patient global, peripheral pain/swelling, duration of morning stiffness and CRP in mg/L. The ASDAScrp is calculated with the following equation: $0.121 \times \text{total back pain} + 0.110 \times \text{patient global} + 0.073 \times \text{peripheral pain/swelling} + 0.058 \times \text{duration of morning stiffness} + 0.579 \times \ln(\text{CRP} + 1)$. CRP is in mg/liter, the range of other variables is from 0(normal) to 10(very severe); Ln represents the natural logarithm). Data from five variables combined to yield a score (0.6361 to no defined upper limit), where higher the score worse the disease activity.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 52 | |

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-----------------------------------|---------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 ^[31] | 94 ^[32] | 102 ^[33] | |
| Units: percentage of participants | | | | |
| number (not applicable) | 8.6 | 29.8 | 27.5 | |

Notes:

[31] - Total participants 105. One participant who did not receive study drug is included in the analysis.

[32] - All randomized participants with baseline ASDAS <2.1.

[33] - All randomized participants with baseline ASDAS <2.1.

Statistical analyses

| Statistical analysis title | Statistical analysis ASDAS Low Disease |
|---|---|
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |
| Number of subjects included in analysis | 198 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[34] |
| P-value | < 0.001 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 4.58 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.02 |
| upper limit | 10.41 |

Notes:

[34] - Total participants 199. One participant who did not receive study drug is included in the analysis.

| Statistical analysis title | Statistical analysis ASDAS Low Disease |
|---|---|
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[35] |
| P-value | < 0.001 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 3.99 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.76 |
| upper limit | 9.05 |

Notes:

[35] - Total participants 207. One participant who did not receive study drug is included in the analysis.

Secondary: Change from Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

| | |
|-----------------|---|
| End point title | Change from Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) |
|-----------------|---|

End point description:

The BASDAI is a participant-reported assessment consisting of 6 questions that relate to 5 major symptoms relevant to axial spondyloarthritis (axSpA): 1) Fatigue, 2) Spinal pain, 3) Peripheral arthritis, 4) Enthesitis, 5) Intensity, and 6) Duration of morning stiffness. Participants need to score each item with a score from 0 to 10 (NRS). Total score is obtained from the average of symptom scores ranging 0 (no problem) to 10 (worst problem), with a higher score indicating more severe AS symptom. LS mean was derived from MMRM with treatment, geographic region, screening MRI/CRP status, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Week 16

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-------------------------------------|---------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 ^[36] | 96 ^[37] | 102 ^[38] | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | -1.51 (± 0.216) | -2.18 (± 0.220) | -2.52 (± 0.217) | |

Notes:

[36] - All randomized participants with evaluable data.

[37] - All randomized participants with evaluable data.

[38] - All randomized participants with evaluable data.

Statistical analyses

| Statistical analysis title | Change from Baseline in BASDAI |
|---|---|
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.031 |
| Method | Mixed models analysis |
| Parameter estimate | LS Means Square Difference |
| Point estimate | -0.67 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.28 |
| upper limit | -0.06 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.308 |

| Statistical analysis title | Change from Baseline in BASDAI |
|----------------------------|---|
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.001 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -1.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.61 |
| upper limit | -0.41 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.305 |

Secondary: Change from Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

| | |
|--|---|
| End point title | Change from Baseline in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) |
| End point description: | |
| The BASDAI is a participant-reported assessment consisting of 6 questions that relate to 5 major symptoms relevant to axial spondyloarthritis (axSpA): 1) Fatigue, 2) Spinal pain, 3) Peripheral arthritis, 4) Enthesitis, 5) Intensity, and 6) Duration of morning stiffness. Participants need to score each item with a score from 0 to 10 (NRS). Total score is obtained from the average of symptom scores ranging 0 (no problem) to 10 (worst problem), with a higher score indicating more severe AS symptom. LS mean was derived from MMRM with treatment, geographic region, screening MRI/CRP status, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 52 | |

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-------------------------------------|---------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 ^[39] | 96 ^[40] | 102 ^[41] | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | -1.76 (± 0.305) | -2.89 (± 0.266) | -3.04 (± 0.266) | |

Notes:

[39] - All randomized participants with evaluable data.

[40] - All randomized participants with evaluable data.

[41] - All randomized participants with evaluable data.

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Change from Baseline in BASDAI |
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.006 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -1.13 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.92 |
| upper limit | -0.33 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.404 |

| | |
|---|---|
| Statistical analysis title | Change from Baseline in BASDAI |
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.002 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -1.29 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.08 |
| upper limit | -0.49 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.404 |

Secondary: Change from Baseline in Magnetic Resonance Imaging (MRI) of the Sacroiliac Joint (SIJ) Spondyloarthritis Research Consortium of Canada (SPARCC) Score

| | |
|-----------------|---|
| End point title | Change from Baseline in Magnetic Resonance Imaging (MRI) of the Sacroiliac Joint (SIJ) Spondyloarthritis Research Consortium of Canada (SPARCC) Score |
|-----------------|---|

End point description:

Both left and right SIJ are scored for bone marrow edema. Each side has 6 slices and each slice has 6 scoring units, and each scoring unit has a score of 0 or 1. Total SIJ SPARCC scores can range from 0 to 72 with higher scores reflecting worse disease. LS Mean was derived from ANCOVA model with treatment, geographic region, screening MRI/CRP status and baseline value as fixed factors.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 16 | |

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-------------------------------------|--------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 90 ^[42] | 85 ^[43] | 92 ^[44] | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | -0.31 (± 0.539) | -3.38 (± 0.549) | -4.52 (± 0.530) | |

Notes:

[42] - All randomized participants with baseline and Week 16 SPARCC score.

[43] - All randomized participants with baseline and Week 16 SPARCC score.

[44] - All randomized participants with baseline and Week 16 SPARCC score.

Statistical analyses

| Statistical analysis title | Statistical analysis MRI SPARCC |
|---|---|
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |
| Number of subjects included in analysis | 175 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | -3.07 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.58 |
| upper limit | -1.57 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.764 |

| Statistical analysis title | Statistical analysis MRI SPARCC |
|---|---|
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |
| Number of subjects included in analysis | 182 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | -4.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.68 |
| upper limit | -2.72 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.751 |

Secondary: Change from Baseline in SPARCC Enthesitis Score

| | |
|---|---|
| End point title | Change from Baseline in SPARCC Enthesitis Score |
| End point description: | |
| <p>The SPARCC enthesitis is an index used to measure the severity of enthesitis. The SPARCC assesses 16 sites for enthesitis using a score of "0" for no activity or "1" for activity. Sites assessed include Medial epicondyle (left/right [L/R]), Lateral epicondyle (L/R), Supraspinatus insertion into greater tuberosity of humerus (L/R), Greater trochanter (L/R), Quadriceps insertion into superior border of patella (L/R), Patellar ligament insertion into inferior pole of patella or tibial tubercle (L/R), Achilles tendon insertion into calcaneum (L/R), and Plantar fascia insertion into calcaneum (L/R). The SPARCC is the sum of all site scores (range 0 to 16). Higher scores indicate more severe enthesitis. LS Mean was derived from MMRM with treatment, geographic region, screening MRI/CRP status, baseline value visit, baseline value-by-visit and treatment-by-visit interaction as fixed factors.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 52 | |

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-------------------------------------|--------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 86 ^[45] | 65 ^[46] | 74 ^[47] | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | -2.87 (± 0.447) | -2.99 (± 0.427) | -3.14 (± 0.407) | |

Notes:

[45] - All randomized participants with a baseline SPARCC score >0.

[46] - All randomized participants with a baseline SPARCC score >0.

[47] - All randomized participants with a baseline SPARCC score >0.

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Change from Baseline in SPARCC Enthesitis Score |
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |
| Number of subjects included in analysis | 151 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.849 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.12 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.35 |
| upper limit | 1.11 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.621 |

| | |
|---|---|
| Statistical analysis title | Change from Baseline in SPARCC Enthesitis Score |
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |
| Number of subjects included in analysis | 160 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.648 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.28 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.48 |
| upper limit | 0.93 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.608 |

Secondary: Change from Baseline in Bath Ankylosing Spondylitis Functional Index (BASFI)

| | |
|--|--|
| End point title | Change from Baseline in Bath Ankylosing Spondylitis Functional Index (BASFI) |
| End point description: | |
| BASFI is a participant-reported assessment that establishes a participant's functional baseline and subsequent response to treatment. Participants were asked to rate the difficulty associated with 10 individual basic functional activities. Participant responded to each question using a NRS scale (range 0 to 10), with a higher score indicating worse functioning. The participant's final BASFI score is the mean of the 10 item scores with the minimum value of 0 and a possible maximum value of 10, with a higher score indicating worse function. LS Mean was derived from MMRM with treatment, geographic region, screening MRI/CRP status, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 52 | |

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-------------------------------------|---------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 ^[48] | 96 ^[49] | 102 ^[50] | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | -1.57 (± 0.333) | -2.63 (± 0.292) | -2.75 (± 0.291) | |

Notes:

[48] - All randomized participants with evaluable data.

[49] - All randomized participants with evaluable data.

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Change from Baseline in BASFI |
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.018 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -1.06 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.93 |
| upper limit | -0.18 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.443 |

| | |
|---|---|
| Statistical analysis title | Change from Baseline in BASFI |
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.008 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -1.18 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.05 |
| upper limit | -0.31 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.442 |

Secondary: Percentage of Participants Achieving ASDAS Inactive Disease

| | |
|--|---|
| End point title | Percentage of Participants Achieving ASDAS Inactive Disease |
| End point description: | |
| ASDAS is a composite index to assess disease activity in axSpA. ASDAS Inactive Disease is defined as a | |

score of less than (<)1.3. The parameters used for the ASDAS (with CRP as acute phase reactant) are total back pain, patient global, peripheral pain/swelling, duration of morning stiffness and CRP in mg/L. The ASDAScrp is calculated with the following equation: $0.121 \times \text{total back pain} + 0.110 \times \text{patient global} + 0.073 \times \text{peripheral pain/swelling} + 0.058 \times \text{duration of morning stiffness} + 0.579 \times \ln(\text{CRP} + 1)$. (CRP is in mg/liter, the range of other variables is from 0(normal) to 10(very severe); Ln represents the natural logarithm). Data from five variables combined to yield a score (0.6361 to no defined upper limit), where higher the score worse the disease activity.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 52 | |

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-----------------------------------|---------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 ^[51] | 96 ^[52] | 102 ^[53] | |
| Units: percentage of participants | | | | |
| number (not applicable) | 2.9 | 13.5 | 10.8 | |

Notes:

[51] - Total participants 105. One participant who did not receive study drug is included in the analysis.

[52] - All randomized participants.

[53] - All randomized participants.

Statistical analyses

| Statistical analysis title | Statistical analysis Achieving ASDAS Inactive |
|---|---|
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[54] |
| P-value | = 0.0011 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 5.33 |
| Confidence interval | |
| level | Other: 96 % |
| sides | 2-sided |
| lower limit | 1.47 |
| upper limit | 19.4 |

Notes:

[54] - Total participants 201. One participant who did not receive study drug is included in the analysis.

| Statistical analysis title | Statistical analysis Achieving ASDAS Inactive |
|---|---|
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[55] |
| P-value | = 0.031 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 4.22 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.14 |
| upper limit | 15.66 |

Notes:

[55] - Total participants 207. One participant who did not receive study drug is included in the analysis.

Secondary: Change from Baseline in the Measure of High Sensitivity C-Reactive Protein (CRP)

| | |
|-----------------|--|
| End point title | Change from Baseline in the Measure of High Sensitivity C-Reactive Protein (CRP) |
|-----------------|--|

End point description:

High-sensitivity C-reactive protein (hs-CRP) was the measure of acute phase reactant and was measured with a high sensitivity assay at the central laboratory to help assess the effect of ixekizumab on disease activity. LS Mean was derived from MMRM with treatment, geographic region, screening MRI/CRP status, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Week 52

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-------------------------------------|---------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 ^[56] | 96 ^[57] | 102 ^[58] | |
| Units: milligram/liter (mg/L) | | | | |
| least squares mean (standard error) | -4.804 (± 2.0370) | -8.611 (± 2.0028) | -7.547 (± 1.9654) | |

Notes:

[56] - All randomized participants with evaluable data.

[57] - All randomized participants with evaluable data.

[58] - All randomized participants with evaluable data.

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Change from Baseline in the CRP |
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.183 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -3.807 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.418 |
| upper limit | 1.804 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.8507 |

| | |
|---|---|
| Statistical analysis title | Change from Baseline in the CRP |
| Comparison groups | Ixekizumab 80 mg Q2W (IXEQ2W) v Placebo |
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.331 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -2.743 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.294 |
| upper limit | 2.807 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.8202 |

Secondary: Change from Baseline in Bath Ankylosing Spondylitis Metrology Index (BASMI)

| | |
|--|---|
| End point title | Change from Baseline in Bath Ankylosing Spondylitis Metrology Index (BASMI) |
| End point description: | |
| <p>Bath Ankylosing Spondylitis Metrology Index (BASMI) is a combined index comprising the following 5 clinical measurements of spinal mobility in participants with axSpA: 1) Lateral spinal flexion 2) Tragus-to-wall distance 3) Lumbar flexion (modified Schrober) 4) Maximal intermalleolar distance, and 5) Cervical rotation. The BASMI includes these 5 measurements that were each scaled to a score of 0 to 10 depending on the result of the assessment (BASMI linear function). The average score of the 5 assessments gives the BASMI linear result. LS Mean was derived from MMRM with treatment, geographic region, screening MRI/CRP status, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 52 | |

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-------------------------------------|---------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 ^[59] | 96 ^[60] | 102 ^[61] | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | -0.17 (± 0.112) | -0.56 (± 0.097) | -0.48 (± 0.097) | |

Notes:

[59] - All randomized participants with evaluable data.

[60] - All randomized participants with evaluable data.

[61] - All randomized participants with evaluable data.

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Change from Baseline in BASMI Statistical Analysis |
| Comparison groups | Ixekizumab 80 mg Q4W (IXEQ4W) v Placebo |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.008 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.69 |
| upper limit | -0.1 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.148 |

| | |
|---|--|
| Statistical analysis title | Change from Baseline in BASMI Statistical Analysis |
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.038 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.31 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.6 |
| upper limit | -0.02 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.148 |

Secondary: Change from Baseline in Chest Expansion

| | |
|-----------------|---|
| End point title | Change from Baseline in Chest Expansion |
|-----------------|---|

End point description:

While participants have their hands resting on or behind the head, the assessor has measured the

chest's encircled length by centimeter at the fourth intercostal level anteriorly. The difference between maximal inspiration and expiration in centimeters was recorded. Two tries were recorded. The better measurement (larger difference) of 2 tries (in centimeters) was used for analyses. LS Mean was derived from MMRM with treatment, geographic region, screening MRI/CRP status, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 52 | |

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-------------------------------------|---------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 ^[62] | 96 ^[63] | 102 ^[64] | |
| Units: centimeter (cm) | | | | |
| least squares mean (standard error) | 0.57 (± 0.253) | 0.62 (± 0.206) | 0.91 (± 0.209) | |

Notes:

[62] - All randomized participants with evaluable data.

[63] - All randomized participants with evaluable data.

[64] - All randomized participants with evaluable data.

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Change from Baseline in Chest Expansion |
| Comparison groups | Ixekizumab 80 mg Q4W (IXEQ4W) v Placebo |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.871 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.05 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.59 |
| upper limit | 0.7 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.325 |

| | |
|-----------------------------------|---|
| Statistical analysis title | Change from Baseline in Chest Expansion |
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.295 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.34 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.3 |
| upper limit | 0.99 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.327 |

Secondary: Change from Baseline in Occiput to Wall Distance

| | |
|--|--|
| End point title | Change from Baseline in Occiput to Wall Distance |
| End point description: | |
| The participant is to make a maximum effort to touch the head against the wall when standing with heels and back against the wall (occiput). Then the distance from occiput to wall is measured. Two tries will be recorded. The better (smaller) measurement of 2 tries (in centimeters) will be used for analyses. LS Mean was derived from MMRM with treatment, geographic region, screening MRI/CRP status, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 52 | |

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-------------------------------------|---------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 ^[65] | 96 ^[66] | 102 ^[67] | |
| Units: cm | | | | |
| least squares mean (standard error) | 0.04 (± 0.312) | -0.42 (± 0.257) | -0.73 (± 0.259) | |

Notes:

[65] - All randomized participants with evaluable data.

[66] - All randomized participants with evaluable data.

[67] - All randomized participants with evaluable data.

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Change from Baseline in Occiput to Wall Distance |
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.257 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.46 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.26 |
| upper limit | 0.34 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.406 |

| | |
|---|--|
| Statistical analysis title | Change from Baseline in Occiput to Wall Distance |
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.057 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.77 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.56 |
| upper limit | 0.02 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.402 |

Secondary: Change from Baseline in Maastricht Ankylosing Spondylitis Enthesitis Score (MASES)

| | |
|-----------------|--|
| End point title | Change from Baseline in Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) |
|-----------------|--|

End point description:

Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) is an index used to measure the severity of enthesitis. The MASES assesses 13 sites for enthesitis using a score of "0" for no activity or "1" for activity. Sites assessed included costochondral 1 (right/left [R/L]), costochondral 7 (R/L), spinal iliaca anterior superior (R/L), crista iliaca (R/L), spina iliaca posterior (R/L), processus spinosus L5, and achilles tendon proximal insertion (R/L). The MASES is the sum of all site scores (range 0 to 13); higher scores indicate more severe enthesitis. LS mean was derived from MMRM with treatment, geographic region, screening MRI/CRP status, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 52 | |

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-------------------------------------|---------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 ^[68] | 96 ^[69] | 102 ^[70] | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | -2.34 (± 0.361) | -3.21 (± 0.342) | -3.19 (± 0.336) | |

Notes:

[68] - All randomized participants with evaluable data.

[69] - All randomized participants with evaluable data.

[70] - All randomized participants with evaluable data.

Statistical analyses

| Statistical analysis title | Change from Baseline in MASES |
|---|---|
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.082 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.87 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.85 |
| upper limit | 0.11 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.496 |

| Statistical analysis title | Change from Baseline in MASES |
|---|---|
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.088 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.85 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.82 |
| upper limit | 0.13 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.493 |

Secondary: Change from Baseline in Severity of Peripheral Arthritis by Tender (TJC) and Swollen Joint Count (SJC) Scores of 44 Joints

| | |
|-----------------|--|
| End point title | Change from Baseline in Severity of Peripheral Arthritis by Tender (TJC) and Swollen Joint Count (SJC) Scores of 44 Joints |
|-----------------|--|

End point description:

The number of tender and painful joints was determined by examination of 46 joints (23 joints on each side of the participants body). The 46 joints are assessed and classified as tender or not tender. Sum of all joints checked to be tender/painful divided by number of evaluable joints which is multiplied by 46 to obtain TJC score. The scores ranges from 0 (no tender/painful joints) to 46 (all joints tender/painful). Swollen joint count SJC was determined by examination of 44 joints (22 joints on each side of the participants body). The joints are classified as swollen or not swollen. Sum of all joints checked to be swollen divided by number of evaluable joints which is multiplied by 44 to obtain SJC score. Score ranges from 0 (not swollen) to 44 (all joints swollen). LS mean was derived from MMRM with treatment, geographic region, screening MRI/CRP status and baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Week 52

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-------------------------------------|---------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 ^[71] | 96 ^[72] | 102 ^[73] | |
| Units: joint counts | | | | |
| least squares mean (standard error) | | | | |
| TJC | -0.59 (± 1.039) | -2.38 (± 0.993) | -4.12 (± 0.916) | |
| SJC | -3.66 (± 0.261) | -4.63 (± 0.237) | -4.41 (± 0.228) | |

Notes:

[71] - TJC number of participants (n) is 83 and a baseline with TJC>0.
SJC n is 50 and baseline with SJC>0

[72] - TJC number of participants is 70 and baseline with TJC>0.
SJC n is 51 and baseline with SJC>0.

[73] - TJC number of participants is 86 and baseline with TJC>0.
SJC n is 57 and baseline with SJC>0.

Statistical analyses

| | |
|----------------------------|--------------------------|
| Statistical analysis title | Statistical analysis TJC |
|----------------------------|--------------------------|

Statistical analysis description:

TJC

| | |
|-------------------|---|
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |
|-------------------|---|

| | |
|---|----------------------------|
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.219 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -1.79 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.66 |
| upper limit | 1.09 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.442 |

| | |
|--|---|
| Statistical analysis title | Statistical analysis TJC |
| Statistical analysis description: TJC | |
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.013 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -3.53 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.3 |
| upper limit | -0.76 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.388 |

| | |
|--|---|
| Statistical analysis title | Statistical analysis SJC |
| Statistical analysis description: SJC | |
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.009 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.97 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.68 |
| upper limit | -0.26 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.355 |

| | |
|--|---|
| Statistical analysis title | Statistical analysis SJC |
| Statistical analysis description: SJC | |
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.034 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.76 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.46 |
| upper limit | -0.06 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.348 |

Secondary: Number of Participants with Anterior Uveitis

| | |
|--|--|
| End point title | Number of Participants with Anterior Uveitis |
| End point description: Number of participants with anterior uveitis. Anterior uveitis is an inflammation of the middle layer of the eye which includes the iris (colored part of the eye) and the adjacent tissue, known as the ciliary body. | |
| End point type | Secondary |
| End point timeframe: Baseline through Week 52 | |

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-------------------------------|---------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 ^[74] | 96 ^[75] | 102 ^[76] | |
| Units: number of participants | | | | |
| number (not applicable) | 2 | 1 | 2 | |

Notes:

[74] - Total participants 105. One participant who did not receive study drug is included in the analysis.

[75] - All randomized participants.

[76] - All randomized participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Fatigue Numeric Rating Scale (NRS) Score

| | |
|-----------------|--|
| End point title | Change from Baseline in the Fatigue Numeric Rating Scale (NRS) Score |
|-----------------|--|

End point description:

The Fatigue Severity NRS is a participant-administered, single-item, 11-point horizontal scale anchored at 0 and 10, with 0 representing "no fatigue" and 10 representing "as bad as you can imagine". Participants rate their fatigue (feeling tired or worn out) by circling the one number that describes their worst level of fatigue during the previous 24 hours. LS Mean was derived from MMRM with treatment, geographic region, screening MRI/CRP status, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Week 52

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-------------------------------------|---------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 ^[77] | 96 ^[78] | 102 ^[79] | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | -2.1 (± 0.38) | -2.6 (± 0.32) | -2.7 (± 0.32) | |

Notes:

[77] - All randomized participants with evaluable data.

[78] - All randomized participants with evaluable data.

[79] - All randomized participants with evaluable data.

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Change from Baseline in the Fatigue NRS |
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.325 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.5 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.5 |
| upper limit | 0.5 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.5 |

| | |
|---|---|
| Statistical analysis title | Change from Baseline in the Fatigue NRS |
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.206 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.6 |
| upper limit | 0.4 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.5 |

Secondary: Change from Baseline in ASAS Health Index (ASAS HI)

| | |
|---|---|
| End point title | Change from Baseline in ASAS Health Index (ASAS HI) |
| End point description: | |
| <p>ASAS-HI is a disease-specific health-index instrument designed to assess the impact of interventions for SpA, including axSpA. The 17-item instrument has scores ranging from 0 (good health) to 17 (poor health). Each item consists of one question that the participant needs to respond to with either "I agree" (score of 1) or "I do not agree" (score of 0). A score of "1" is given where the item is affirmed, indicating adverse health. All item scores are summed to give a total score or index. LS Mean was derived MMRM with treatment, geographic region, screening MRI/CRP status, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 52 | |

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-------------------------------------|---------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 ^[80] | 96 ^[81] | 102 ^[82] | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | -2.57 (± 0.455) | -3.16 (± 0.395) | -3.54 (± 0.396) | |

Notes:

[80] - All randomized participants with evaluable data.

[81] - All randomized participants with evaluable data.

[82] - All randomized participants with evaluable data.

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Change from Baseline in ASAS Health Index |
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.33 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.59 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.77 |
| upper limit | 0.6 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.601 |

| | |
|---|---|
| Statistical analysis title | Change from Baseline in ASAS Health Index |
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.11 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.97 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.15 |
| upper limit | 0.22 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.602 |

Secondary: Change from Baseline in the Jenkins Sleep Evaluation Questionnaire (JSEQ)

| | |
|-----------------|---|
| End point title | Change from Baseline in the Jenkins Sleep Evaluation Questionnaire (JSEQ) |
|-----------------|---|

End point description:

Jenkins Sleep Evaluation Questionnaire (JSEQ) is a 4 item scale designed to estimate sleep problems in clinical research. The JSEQ assesses the frequency of sleep disturbance in 4 categories: 1) trouble falling asleep, 2) waking up several times during the night, 3) having trouble staying asleep (including waking up far too early), and 4) waking up after the usual amount of sleep feeling tired and worn out. Patients report the numbers of days they experience each of these problems in the past month on a 6 point Likert Scale ranging from 0 = "no days" to 5 = "22-30 days". The total JSEQ score ranges from 0 to 20, with higher scores indicating greater sleep disturbance. LS Mean was derived from using MMRM with treatment, geographic region, screening MRI/CRP status, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline, Week 52

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-------------------------------------|---------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 ^[83] | 96 ^[84] | 102 ^[85] | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | -2.9 (± 0.63) | -3.6 (± 0.52) | -3.6 (± 0.53) | |

Notes:

[83] - All randomized participants with evaluable data.

[84] - All randomized participants with evaluable data.

[85] - All randomized participants with evaluable data.

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Change from Baseline in the JSEQ |
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.348 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.4 |
| upper limit | 0.8 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.81 |

| | |
|---|---|
| Statistical analysis title | Change from Baseline in the JSEQ |
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.386 |
| Method | Mixed models analysis |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.3 |
| upper limit | 0.9 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.82 |

Secondary: Change from Baseline in the Work Productivity Activity Impairment Spondyloarthritis (WPAI-SpA) Scores

| | |
|--|---|
| End point title | Change from Baseline in the Work Productivity Activity Impairment Spondyloarthritis (WPAI-SpA) Scores |
| End point description: | |
| <p>The WPAI-SpA consists of 6 questions to determine employment status, hours missed from work because of SpA, hours missed from work for other reasons, hours actually worked, the degree to which SpA affected work productivity while at work, and the degree to which SpA affected activities outside of work. The WPAI-SpA has been validated in the rad-axSpA patient population. Four scores are derived: percentage of absenteeism, percentage of presenteeism (reduced productivity while at work), an overall work impairment score that combines absenteeism and presenteeism, and percentage of impairment in activities performed outside of work. The computed percentage range for each sub-scale was from 0-100, with higher scores indicating greater impairment and less productivity. LS Mean was derived from ANCOVA with treatment, geographic region, screening MRI/CRP status and baseline value.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 52 | |

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|-------------------------------------|---------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 104 ^[86] | 96 ^[87] | 102 ^[88] | |
| Units: score on a scale | | | | |
| least squares mean (standard error) | | | | |
| Overall Impairment Score | -13.20 (± 3.386) | -26.96 (± 3.439) | -19.49 (± 3.221) | |
| Percentage of absenteeism | -3.11 (± 2.215) | -9.01 (± 2.257) | -7.26 (± 2.151) | |

| | | | | |
|--|-----------------------|-----------------------|-----------------------|--|
| Percentage of presenteeism | -12.40 (\pm 3.200) | -26.01 (\pm 3.245) | -18.61 (\pm 3.047) | |
| Percentage of impairment in activities | -14.42 (\pm 2.584) | -25.05 (\pm 2.617) | -24.41 (\pm 2.567) | |

Notes:

[86] - All randomized participants with evaluable data.

[87] - All randomized participants with evaluable data.

[88] - All randomized participants with evaluable data.

Statistical analyses

| Statistical analysis title | Statistical analysis WPAI Overall Impairment Score |
|---|--|
| Statistical analysis description: | |
| Overall Impairment Score | |
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.005 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | -13.76 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -23.32 |
| upper limit | -4.2 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 4.835 |

| Statistical analysis title | Statistical analysis WPAI Overall Impairment Score |
|---|--|
| Statistical analysis description: | |
| Overall Impairment Score | |
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.183 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | -6.29 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -15.58 |
| upper limit | 3 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 4.697 |

| | |
|---|--|
| Statistical analysis title | Statistical analysis WPAI Percentage Absenteeism |
| Statistical analysis description: | |
| Percentage of absenteeism | |
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.06 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | -5.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -12.05 |
| upper limit | 0.26 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.114 |

| | |
|---|--|
| Statistical analysis title | Statistical analysis WPAI Percentage Absenteeism |
| Statistical analysis description: | |
| Percentage of absenteeism | |
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.182 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | -4.15 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.27 |
| upper limit | 1.97 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.098 |

| | |
|-----------------------------------|--|
| Statistical analysis title | Statistical analysis WPAI Percentage Presentisms |
| Statistical analysis description: | |
| Percentage of presentisms | |
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.003 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | -13.61 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -22.62 |
| upper limit | -4.6 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 4.558 |

| | |
|---|--|
| Statistical analysis title | Statistical analysis WPAI Percentage Presentisms |
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.164 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | -6.21 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -15 |
| upper limit | 2.58 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 4.446 |

| | |
|--|--|
| Statistical analysis title | Statistical analysis WPAI Percentage of Impairment |
| Statistical analysis description: | |
| Percentage of Impairment in Activities Performed Outside of Work | |
| Comparison groups | Placebo v Ixekizumab 80 mg Q4W (IXEQ4W) |
| Number of subjects included in analysis | 200 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.004 |
| Method | LS Mean Difference |
| Parameter estimate | LS Mean Difference |
| Point estimate | -10.63 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -17.85 |
| upper limit | -3.41 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.669 |

| | |
|---|--|
| Statistical analysis title | Statistical analysis WPAI Percentage of Impairment |
| Comparison groups | Placebo v Ixekizumab 80 mg Q2W (IXEQ2W) |
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.006 |
| Method | ANCOVA |
| Parameter estimate | LS Mean Difference |
| Point estimate | -9.99 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -17.12 |
| upper limit | -2.86 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.621 |

Secondary: Change from Baseline in ASAS-Nonsteroidal Anti-Inflammatory Drug (NSAID) Score

| | |
|--|--|
| End point title | Change from Baseline in ASAS-Nonsteroidal Anti-Inflammatory Drug (NSAID) Score |
| End point description: | |
| ASAS-NSAID score is used to present the NSAID intake by considering the type of NSAID, the total dose, & the number of days taking NSAID during a period of interest (PI). For NSAID equivalent scoring system, range is from 0 to 100, the higher the score, the greater the NSAID intake. ASAS-NSAID score=(equivalent NSAID score) x (days of intake during PI) x (days per week)/(PI in days). | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 52 | |

| End point values | Placebo | Ixekizumab 80 mg Q4W (IXEQ4W) | Ixekizumab 80 mg Q2W (IXEQ2W) | |
|--------------------------------------|--------------------|-------------------------------|-------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 96 ^[89] | 81 ^[90] | 95 ^[91] | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | -8.89 (± 29.986) | -7.91 (± 34.257) | -5.33 (± 20.935) | |

Notes:

[89] - All randomized participants who had NSAID (including COX-2 Inhibitor) intake at Baseline.

[90] - All randomized participants who had NSAID (including COX-2 Inhibitor) intake at Baseline.

[91] - All randomized participants who had NSAID (including COX-2 Inhibitor) intake at Baseline.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment Emergent (TE) Anti-Ixekizumab Antibodies

| | |
|-----------------|--|
| End point title | Number of Participants with Treatment Emergent (TE) Anti-Ixekizumab Antibodies |
|-----------------|--|

End point description:

A treatment-emergent positive anti-drug antibody (TE-ADA+) participant will be defined as a 4-fold increase over a positive baseline antibody titer (Tier 3); or for a negative baseline titer, a participant with an increase from the baseline to a level of $\geq 1:10$. All randomized participant who received at least one dose of ixekizumab during the study and had an evaluable baseline sample and at least 1 evaluable post baseline sample.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 52

| End point values | IXE80Q2W-Q2W | IXE80Q4W-Q4W | PBO-IXE80Q2W | IXE80Q4W-Q2W |
|-----------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 102 ^[92] | 56 ^[93] | 62 ^[94] | 40 ^[95] |
| Units: participants | | | | |
| number (not applicable) | 14 | 5 | 8 | 2 |

Notes:

[92] - All randomized participant who received drug and had evaluable post baseline data.

[93] - All randomized participant who received drug and had evaluable post baseline data.

[94] - All randomized participant who received drug and had evaluable post baseline data.

[95] - All randomized participant who received drug and had evaluable post baseline data.

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Trough Concentration at Steady State (C_{trough ss})

| | |
|-----------------|---|
| End point title | Pharmacokinetics (PK): Trough Concentration at Steady State (C _{trough ss}) |
|-----------------|---|

End point description:

PK trough serum concentration samples were collected at steady state (C_{trough ss}). Geometric Coefficient Variation (CV) is a percent.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 52

| End point values | IXEQ2W (80S)/IXEQ2W | IXEQ2W (80S)/IXEQ2W Open Label | IXEQ2W (160S)/IXEQ2W | IXEQ2W (160s)/IXEQ2W Open Label |
|---|----------------------|--------------------------------|----------------------|---------------------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 32 ^[96] | 18 ^[97] | 28 ^[98] | 24 ^[99] |
| Units: microgram/milliliter (µg/mL) | | | | |
| geometric mean (geometric coefficient of variation) | 7.88 (± 73) | 9.56 (± 60) | 10.3 (± 61) | 10.4 (± 72) |

Notes:

[96] - All randomized participants who had evaluable PK data. Geometric CV is a percent.

[97] - All randomized participants who had evaluable PK data. Geometric CV is a percent.

[98] - All randomized participants who had evaluable PK data. Geometric CV is a percent.

[99] - All randomized participants who had evaluable PK data. Geometric CV is a percent.

| End point values | IXEQ4W (80S) IXEQ4W | IXEQ4W (80S)/IXEQ2W Open Label | IXEQ4W (160S)/IXEQ4W | IXEQ4W (160S) IXEQ2W Open Label |
|---|----------------------|--------------------------------|----------------------|---------------------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 28 ^[100] | 19 ^[101] | 28 ^[102] | 21 ^[103] |
| Units: microgram/milliliter (µg/mL) | | | | |
| geometric mean (geometric coefficient of variation) | 2.88 (± 49) | 6.45 (± 124) | 3.54 (± 79) | 11.5 (± 53) |

Notes:

[100] - All randomized participants who had evaluable PK data. Geometric CV is a percent.

[101] - All randomized participants who had evaluable PK data. Geometric CV is a percent.

[102] - All randomized participants who had evaluable PK data. Geometric CV is a percent.

[103] - All randomized participants who had evaluable PK data. Geometric CV is a percent.

| End point values | PBO/IXEQ2W Open Label | | | |
|---|-----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 55 ^[104] | | | |
| Units: microgram/milliliter (µg/mL) | | | | |
| geometric mean (geometric coefficient of variation) | 9.25 (± 66) | | | |

Notes:

[104] - All randomized participants who had evaluable PK data. Geometric CV is a percent.

Statistical analyses

No statistical analyses for this end point

Secondary: (PK): Trough Concentration at Steady State (C_{trough ss})

End point title (PK): Trough Concentration at Steady State (C_{trough ss})

End point description:

End point type Secondary

End point timeframe:

Week 16

| End point values | IXEQ2W(80S) | IXEQ2W(160S) | IXEQ4W(80S) | IXEQ4W(160S) |
|---|----------------------|----------------------|----------------------|----------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 50 ^[105] | 52 ^[106] | 47 ^[107] | 49 ^[108] |
| Units: µg/mL | | | | |
| geometric mean (geometric coefficient of variation) | 8.76 (± 84) | 10.6 (± 57) | 3.20 (± 52) | 3.46 (± 119) |

Notes:

[105] - All randomized participants who had evaluable PK data. Geometric CV is percent.

[106] - All randomized participants who had evaluable PK data. Geometric CV is a percent.

[107] - All randomized participants who had evaluable PK data. Geometric CV is a percent.

[108] - All randomized participants who had evaluable PK data. Geometric CV is a percent.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 64 Weeks

Adverse event reporting additional description:

All randomized participants who received at least one dose of study drug during the study. There are gender specific adverse events, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 22.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|----------------------|
| Reporting group title | Ixekizumab 80 mg Q2W |
|-----------------------|----------------------|

| | |
|--------------------------------|--|
| Reporting group description: - | |
|--------------------------------|--|

| | |
|-----------------------|----------------------|
| Reporting group title | Ixekizumab 80 mg Q4W |
|-----------------------|----------------------|

| | |
|--------------------------------|--|
| Reporting group description: - | |
|--------------------------------|--|

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

| | |
|--------------------------------|--|
| Reporting group description: - | |
|--------------------------------|--|

| | |
|-----------------------|-----------------------------------|
| Reporting group title | IXE80Q2W IR/IXE80Q2W - Open Label |
|-----------------------|-----------------------------------|

| | |
|--------------------------------|--|
| Reporting group description: - | |
|--------------------------------|--|

| | |
|-----------------------|-----------------------------------|
| Reporting group title | IXE80Q4W IR/IXE80Q2W - Open Label |
|-----------------------|-----------------------------------|

| | |
|--------------------------------|--|
| Reporting group description: - | |
|--------------------------------|--|

| | |
|-----------------------|----------------------------|
| Reporting group title | PBO IR/IXEQ2W - Open Label |
|-----------------------|----------------------------|

| | |
|--------------------------------|--|
| Reporting group description: - | |
|--------------------------------|--|

| | |
|-----------------------|-----------------------------|
| Reporting group title | Other Biologic - Open Label |
|-----------------------|-----------------------------|

| | |
|--------------------------------|--|
| Reporting group description: - | |
|--------------------------------|--|

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

| | |
|--------------------------------|--|
| Reporting group description: - | |
|--------------------------------|--|

| | |
|-----------------------|----------------------|
| Reporting group title | Ixekizumab 80 mg Q4W |
|-----------------------|----------------------|

| | |
|--------------------------------|--|
| Reporting group description: - | |
|--------------------------------|--|

| | |
|-----------------------|----------------------|
| Reporting group title | Ixekizumab 80 mg Q2W |
|-----------------------|----------------------|

| | |
|--------------------------------|--|
| Reporting group description: - | |
|--------------------------------|--|

| | |
|-----------------------|--------------------------|
| Reporting group title | Other Biologic Treatment |
|-----------------------|--------------------------|

| | |
|--------------------------------|--|
| Reporting group description: - | |
|--------------------------------|--|

| Serious adverse events | Ixekizumab 80 mg Q2W | Ixekizumab 80 mg Q4W | Placebo |
|---|----------------------|----------------------|-----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 102 (0.98%) | 2 / 96 (2.08%) | 1 / 104 (0.96%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Nervous system disorders | | | |
| focal dyscognitive seizures | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 102 (0.00%) | 0 / 96 (0.00%) | 0 / 104 (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 |
| Immune system disorders | | | |
| anaphylactoid reaction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 102 (0.00%) | 0 / 96 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| abdominal pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 102 (0.00%) | 1 / 96 (1.04%) | 0 / 104 (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 |
| Psychiatric disorders | | | |
| major depression | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 102 (0.98%) | 0 / 96 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| somatic symptom disorder | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 102 (0.00%) | 0 / 96 (0.00%) | 0 / 104 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| axial spondyloarthritis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 102 (0.00%) | 0 / 96 (0.00%) | 0 / 104 (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 |
| intervertebral disc protrusion | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 102 (0.00%) | 0 / 96 (0.00%) | 0 / 104 (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 |
| osteoarthritis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 102 (0.00%) | 0 / 96 (0.00%) | 0 / 104 (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 |
| Infections and infestations | | | |
| erysipelas | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 102 (0.00%) | 1 / 96 (1.04%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| sinusitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 102 (0.00%) | 0 / 96 (0.00%) | 0 / 104 (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 | IXE80Q2W IR/IXE80Q2W - Open Label | IXE80Q4W IR/IXE80Q2W - Open Label | PBO IR/IXEQ2W - Open Label |
|---|---|---|-------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 40 (0.00%) | 2 / 62 (3.23%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Nervous system disorders | | | |
| focal dyscognitive seizures | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 40 (0.00%) | 0 / 62 (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 |
| Immune system disorders | | | |
| anaphylactoid reaction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 40 (0.00%) | 0 / 62 (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 | | | |
| abdominal pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 40 (0.00%) | 0 / 62 (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 |
| Psychiatric disorders | | | |
| major depression | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 40 (0.00%) | 0 / 62 (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 |
| somatic symptom disorder | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 40 (0.00%) | 0 / 62 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| axial spondyloarthritis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 40 (0.00%) | 0 / 62 (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 |
| intervertebral disc protrusion | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 40 (0.00%) | 1 / 62 (1.61%) |
| 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 | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 40 (0.00%) | 1 / 62 (1.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| erysipelas | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 40 (0.00%) | 0 / 62 (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 |
| sinusitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 40 (0.00%) | 1 / 62 (1.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Other Biologic - Open Label | Placebo | Ixekizumab 80 mg Q4W |
|---|-----------------------------|---------------|----------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 3 (0.00%) | 0 / 5 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Nervous system disorders | | | |
| focal dyscognitive seizures | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 3 (0.00%) | 0 / 5 (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 |
| Immune system disorders | | | |
| anaphylactoid reaction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 3 (0.00%) | 0 / 5 (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 | | | |
| abdominal pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 3 (0.00%) | 0 / 5 (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 |
| Psychiatric disorders | | | |
| major depression | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 3 (0.00%) | 0 / 5 (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 |
| somatic symptom disorder | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 3 (0.00%) | 0 / 5 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| axial spondyloarthritis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 3 (0.00%) | 0 / 5 (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 |
| intervertebral disc protrusion | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 3 (0.00%) | 0 / 5 (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 |
| osteoarthritis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 3 (0.00%) | 0 / 5 (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 |
| Infections and infestations | | | |
| erysipelas | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 3 (0.00%) | 0 / 5 (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 |
| sinusitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 3 (0.00%) | 0 / 5 (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 | Ixekizumab 80 mg Q2W | Other Biologic Treatment | |
|---|-----------------------------|---------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 5 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Nervous system disorders | | | |
| focal dyscognitive seizures | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 5 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| anaphylactoid reaction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 5 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| abdominal pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 5 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| major depression | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|----------------|---------------|--|
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 5 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| somatic symptom disorder alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 5 (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 | | | |
| axial spondyloarthritis alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 5 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| intervertebral disc protrusion alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 5 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| osteoarthritis alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 5 (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 | | | |
| erysipelas alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 5 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| sinusitis alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|----------------|---------------|--|
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 5 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Ixekizumab 80 mg Q2W | Ixekizumab 80 mg Q4W | Placebo |
|---|-------------------------|-------------------------|-------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 47 / 102 (46.08%) | 43 / 96 (44.79%) | 31 / 104 (29.81%) |
| Vascular disorders | | | |
| hypertension | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 4 / 102 (3.92%) | 6 / 96 (6.25%) | 3 / 104 (2.88%) |
| occurrences (all) | 4 | 7 | 3 |
| Nervous system disorders | | | |
| headache | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 5 / 102 (4.90%) | 7 / 96 (7.29%) | 4 / 104 (3.85%) |
| occurrences (all) | 5 | 7 | 4 |
| General disorders and administration site conditions | | | |
| influenza like illness | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 102 (0.00%) | 0 / 96 (0.00%) | 2 / 104 (1.92%) |
| occurrences (all) | 0 | 0 | 4 |
| injection site erythema | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 4 / 102 (3.92%) | 3 / 96 (3.13%) | 1 / 104 (0.96%) |
| occurrences (all) | 11 | 7 | 3 |
| injection site reaction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 17 / 102 (16.67%) | 11 / 96 (11.46%) | 4 / 104 (3.85%) |
| occurrences (all) | 56 | 24 | 7 |
| Eye disorders | | | |
| iritis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|--|-------------------------|------------------------|-----------------------|
| subjects affected / exposed occurrences (all) | 0 / 102 (0.00%) 0 | 0 / 96 (0.00%) 0 | 0 / 104 (0.00%) 0 |
| Gastrointestinal disorders abdominal pain upper alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 1 / 102 (0.98%) 1 | 1 / 96 (1.04%) 1 | 1 / 104 (0.96%) 1 |
| nausea alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 1 / 102 (0.98%) 1 | 1 / 96 (1.04%) 1 | 1 / 104 (0.96%) 1 |
| Respiratory, thoracic and mediastinal disorders oropharyngeal pain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 5 / 102 (4.90%) 7 | 1 / 96 (1.04%) 1 | 0 / 104 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders back pain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 2 / 102 (1.96%) 2 | 3 / 96 (3.13%) 3 | 2 / 104 (1.92%) 2 |
| Infections and infestations bacterial vaginosis alternative dictionary used: MedDRA 22.0 subjects affected / exposed ^[1] occurrences (all) | 0 / 53 (0.00%) 0 | 1 / 46 (2.17%) 1 | 0 / 61 (0.00%) 0 |
| bronchitis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 2 / 102 (1.96%) 2 | 7 / 96 (7.29%) 7 | 3 / 104 (2.88%) 4 |
| nasopharyngitis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 16 / 102 (15.69%) 27 | 18 / 96 (18.75%) 26 | 8 / 104 (7.69%) 11 |
| pharyngitis | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 102 (1.96%) | 4 / 96 (4.17%) | 4 / 104 (3.85%) |
| occurrences (all) | 2 | 5 | 4 |
| sinusitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 102 (1.96%) | 2 / 96 (2.08%) | 1 / 104 (0.96%) |
| occurrences (all) | 2 | 2 | 1 |
| upper respiratory tract infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 6 / 102 (5.88%) | 4 / 96 (4.17%) | 4 / 104 (3.85%) |
| occurrences (all) | 7 | 4 | 4 |
| vulvovaginal mycotic infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed ^[2] | 0 / 53 (0.00%) | 1 / 46 (2.17%) | 0 / 61 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| Non-serious adverse events | IXE80Q2W IR/IXE80Q2W - Open Label | IXE80Q4W IR/IXE80Q2W - Open Label | PBO IR/IXEQ2W - Open Label |
|--|---|---|-------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 13 / 42 (30.95%) | 15 / 40 (37.50%) | 26 / 62 (41.94%) |
| Vascular disorders | | | |
| hypertension | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 1 / 40 (2.50%) | 0 / 62 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Nervous system disorders | | | |
| headache | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 1 / 40 (2.50%) | 1 / 62 (1.61%) |
| occurrences (all) | 1 | 1 | 1 |
| General disorders and administration site conditions | | | |
| influenza like illness | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 40 (0.00%) | 0 / 62 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| injection site erythema | | | |

| | | | |
|--|----------------------|----------------------|------------------------|
| alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 2 / 42 (4.76%) 5 | 0 / 40 (0.00%) 0 | 5 / 62 (8.06%) 6 |
| injection site reaction alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 3 / 42 (7.14%) 11 | 3 / 40 (7.50%) 28 | 11 / 62 (17.74%) 63 |
| Eye disorders iritis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 42 (0.00%) 0 | 0 / 40 (0.00%) 0 | 0 / 62 (0.00%) 0 |
| Gastrointestinal disorders abdominal pain upper alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 42 (0.00%) 0 | 3 / 40 (7.50%) 3 | 0 / 62 (0.00%) 0 |
| nausea alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 4 / 42 (9.52%) 4 | 2 / 40 (5.00%) 2 | 0 / 62 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders oropharyngeal pain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 1 / 42 (2.38%) 1 | 0 / 40 (0.00%) 0 | 0 / 62 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders back pain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 42 (0.00%) 0 | 0 / 40 (0.00%) 0 | 0 / 62 (0.00%) 0 |
| Infections and infestations bacterial vaginosis alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed ^[1] | 0 / 28 (0.00%) | 1 / 15 (6.67%) | 2 / 41 (4.88%) |
| occurrences (all) | 0 | 1 | 2 |
| bronchitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 1 / 40 (2.50%) | 5 / 62 (8.06%) |
| occurrences (all) | 1 | 1 | 5 |
| nasopharyngitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 42 (4.76%) | 7 / 40 (17.50%) | 6 / 62 (9.68%) |
| occurrences (all) | 3 | 10 | 8 |
| pharyngitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 42 (4.76%) | 3 / 40 (7.50%) | 3 / 62 (4.84%) |
| occurrences (all) | 2 | 3 | 3 |
| sinusitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 42 (7.14%) | 1 / 40 (2.50%) | 1 / 62 (1.61%) |
| occurrences (all) | 3 | 1 | 1 |
| upper respiratory tract infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 42 (4.76%) | 3 / 40 (7.50%) | 4 / 62 (6.45%) |
| occurrences (all) | 2 | 4 | 5 |
| vulvovaginal mycotic infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed ^[2] | 0 / 28 (0.00%) | 1 / 15 (6.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| Non-serious adverse events | Other Biologic - Open Label | Placebo | Ixekizumab 80 mg Q4W |
|--|--------------------------------|----------------|-------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 3 / 5 (60.00%) | 1 / 3 (33.33%) | 1 / 5 (20.00%) |
| Vascular disorders | | | |
| hypertension | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | 0 / 3 (0.00%) | 0 / 5 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|--|---|--|
| Nervous system disorders headache alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 5 (0.00%) 0 |
| General disorders and administration site conditions influenza like illness alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) injection site erythema alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) injection site reaction alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 | 1 / 3 (33.33%) 1 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 | 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 |
| Eye disorders iritis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 5 (20.00%) 1 |
| Gastrointestinal disorders abdominal pain upper alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) nausea alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0 | 0 / 5 (0.00%) 0 0 / 5 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders oropharyngeal pain alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|--|---------------------|---------------------|--------------------|
| subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | 0 / 3 (0.00%) 0 | 0 / 5 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders back pain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | 0 / 3 (0.00%) 0 | 0 / 5 (0.00%) 0 |
| Infections and infestations bacterial vaginosis alternative dictionary used: MedDRA 22.0 subjects affected / exposed ^[1] occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 1 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| bronchitis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 5 (0.00%) 0 |
| nasopharyngitis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | 0 / 3 (0.00%) 0 | 0 / 5 (0.00%) 0 |
| pharyngitis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 1 / 3 (33.33%) 1 | 0 / 5 (0.00%) 0 |
| sinusitis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 5 (0.00%) 0 |
| upper respiratory tract infection alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | 0 / 3 (0.00%) 0 | 0 / 5 (0.00%) 0 |
| vulvovaginal mycotic infection alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|--|---------------|---------------|---------------|
| subjects affected / exposed ^[2] | 0 / 4 (0.00%) | 0 / 1 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| Non-serious adverse events | Ixekizumab 80 mg Q2W | Other Biologic Treatment | |
|---|----------------------|--------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 5 (0.00%) | |
| Vascular disorders | | | |
| hypertension | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Nervous system disorders | | | |
| headache | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| General disorders and administration site conditions | | | |
| influenza like illness | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| injection site erythema | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| injection site reaction | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Eye disorders | | | |
| iritis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Gastrointestinal disorders | | | |

| | | | |
|--|---------------------|--------------------|--|
| abdominal pain upper alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 0 / 5 (0.00%) 0 | |
| nausea alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 0 / 5 (0.00%) 0 | |
| Respiratory, thoracic and mediastinal disorders oropharyngeal pain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 0 / 5 (0.00%) 0 | |
| Musculoskeletal and connective tissue disorders back pain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 0 / 5 (0.00%) 0 | |
| Infections and infestations bacterial vaginosis alternative dictionary used: MedDRA 22.0 subjects affected / exposed ^[1] occurrences (all) | 0 / 19 (0.00%) 0 | 0 / 4 (0.00%) 0 | |
| bronchitis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 0 / 5 (0.00%) 0 | |
| nasopharyngitis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 0 / 28 (0.00%) 0 | 0 / 5 (0.00%) 0 | |
| pharyngitis alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|----------------|---------------|--|
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| sinusitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 28 (0.00%) | 0 / 5 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| upper respiratory tract infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| vulvovaginal mycotic infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed ^[2] | 0 / 19 (0.00%) | 0 / 4 (0.00%) | |
| occurrences (all) | 0 | 0 | |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male and female subjects. The number of subjects exposed has been adjusted accordingly.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male and female subjects. The number of subjects exposed has been adjusted accordingly.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 05 October 2018 | There are now two primary objectives to accommodate regional regulatory requirements. One secondary objective was added as a primary objective. Power estimations were added for this objective. Clarified that screening MRI/CRP status was used and not baseline. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported