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	Investigator, Subject

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)/Ixekizumab 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	Ixekizumab
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	Ixekizumab 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	Ixekizumab
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	Ixekizumab
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)/Ixekizumab 80 mg Q2W	Ixekizumab 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	Ixekizumab 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	Ixekizumab 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 ixe 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 (≥)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 (≥)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 × total back pain + 0.110×patient global + 0.073 × peripheral pain/swelling + 0.058 × duration of morning stiffness + 0.579 × Ln(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 × total back pain + 0.110 × patient global + 0.073 × peripheral pain/swelling + 0.058 × duration of morning stiffness + 0.579 × Ln(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 (± 0.7999)	8.0612 (± 0.8129)	7.9600 (± 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 (± 1.2459)	8.9211 (± 1.0783)	9.3291 (± 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×total back pain+0.110×patient global+0.073×peripheral pain/swelling+0.058×duration of morning stiffness+0.579×Ln(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×total back pain+0.110×patient global+0.073×peripheral pain/swelling+0.058×duration of morning stiffness+0.579×Ln(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:

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.

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.

[50] - 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×total back pain+0.110×patient global+0.073×peripheral pain/swelling+0.058×duration of morning stiffness+0.579×Ln(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:

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.

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:

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.

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:

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.

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 (± 3.200)	-26.01 (± 3.245)	-18.61 (± 3.047)	
Percentage of impairment in activities	-14.42 (± 2.584)	-25.05 (± 2.617)	-24.41 (± 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 ≥ 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 (Ctrough ss)

End point title	Pharmacokinetics (PK): Trough Concentration at Steady State (Ctrough ss)

End point description:

PK trough serum concentration samples were collected at steady state (Ctrough 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 (Ctrough ss)

End point title	(PK): Trough Concentration at Steady State (Ctrough 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	0 / 102 (0.00%)	0 / 96 (0.00%)	0 / 104 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
abdominal pain upper			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 102 (0.98%)	1 / 96 (1.04%)	1 / 104 (0.96%)
occurrences (all)	1	1	1
nausea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 102 (0.98%)	1 / 96 (1.04%)	1 / 104 (0.96%)
occurrences (all)	1	1	1
Respiratory, thoracic and mediastinal disorders			
oropharyngeal pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	5 / 102 (4.90%)	1 / 96 (1.04%)	0 / 104 (0.00%)
occurrences (all)	7	1	0
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 102 (1.96%)	3 / 96 (3.13%)	2 / 104 (1.92%)
occurrences (all)	2	3	2
Infections and infestations			
bacterial vaginosis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed[1]	0 / 53 (0.00%)	1 / 46 (2.17%)	0 / 61 (0.00%)
occurrences (all)	0	1	0
bronchitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 102 (1.96%)	7 / 96 (7.29%)	3 / 104 (2.88%)
occurrences (all)	2	7	4
nasopharyngitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	16 / 102 (15.69%)	18 / 96 (18.75%)	8 / 104 (7.69%)
occurrences (all)	27	26	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	2 / 42 (4.76%)	0 / 40 (0.00%)	5 / 62 (8.06%)
occurrences (all)	5	0	6
injection site reaction			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 42 (7.14%)	3 / 40 (7.50%)	11 / 62 (17.74%)
occurrences (all)	11	28	63
Eye disorders			
iritis			
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
Gastrointestinal disorders			
abdominal pain upper			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 42 (0.00%)	3 / 40 (7.50%)	0 / 62 (0.00%)
occurrences (all)	0	3	0
nausea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	4 / 42 (9.52%)	2 / 40 (5.00%)	0 / 62 (0.00%)
occurrences (all)	4	2	0
Respiratory, thoracic and mediastinal disorders			
oropharyngeal pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 42 (2.38%)	0 / 40 (0.00%)	0 / 62 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
back pain			
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
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	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
influenza like illness			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
injection site erythema			
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
injection site reaction			
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
Eye disorders			
iritis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
abdominal pain upper			
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
nausea			
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
Respiratory, thoracic and mediastinal disorders			
oropharyngeal pain			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
bacterial vaginosis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed[1]	0 / 4 (0.00%)	0 / 1 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
bronchitis			
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
nasopharyngitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
pharyngitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
sinusitis			
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
upper respiratory tract infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	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	0 / 28 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
nausea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
oropharyngeal pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
bacterial vaginosis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed[1]	0 / 19 (0.00%)	0 / 4 (0.00%)	
occurrences (all)	0	0	
bronchitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
nasopharyngitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 28 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	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