Clinical trial results:
A Multicenter, Randomized, Double-Blind, Placebo-Controlled 16 Week Study Followed by Long Term Evaluation of Efficacy and Safety of Ixekizumab (LY2439821) in TNFi-Experienced Patients with Radiographic Axial Spondyloarthritis

Summary

EudraCT number	2015-003937-84
Trial protocol	GB FI NL DE ES PL FR IT
Global end of trial date	03 May 2019

Results information

Result version number	v1 (current)
This version publication date	26 January 2020
First version publication date	26 January 2020

Trial information

Trial identification

Sponsor protocol code	I1F-MC-RHBW

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02696798
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 16179

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	03 May 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 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 efficacy and safety of ixekizumab in tumor necrosis factor (TNF) inhibitor-experienced participants with radiographic axial spondyloarthritis (rad-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	12 April 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	Puerto Rico: 7
Country: Number of subjects enrolled	Argentina: 18
Country: Number of subjects enrolled	United States: 40
Country: Number of subjects enrolled	United Kingdom: 20
Country: Number of subjects enrolled	Spain: 14
Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	Korea, Republic of: 34
Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	Finland: 5
Country: Number of subjects enrolled	Brazil: 28
Country: Number of subjects enrolled	Poland: 66
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Mexico: 39
Country: Number of subjects enrolled	Israel: 16
Country: Number of subjects enrolled	France: 17
Country: Number of subjects enrolled	Germany: 1
Worldwide total number of subjects	316
EEA total number of subjects	128

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)	292
From 65 to 84 years	24
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Blinded Treatment Dosing Period (Week 0 to Week 16), Extended Treatment Period (Week 16 to Week 52) followed by post-treatment follow-up period occurring from last treatment visit (week 52), or Early Termination Visit (ETV) up to a minimum of 12 weeks following that visit.

Pre-assignment

Screening details:

Participants who completed study were eligible to enroll into a long-term study (I1F-MC-RHBY [2016-002634-69]) for up to 2 additional years. Participants who terminate study RHBW early or who do not enroll into Study RHBY will complete the Post-Treatment Follow-Up (PTFU) Period in study RHBW.

Period 1

Period 1 title	Blinded Treatment Dosing Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo (PBO)

Arm description:

Participants received placebo every two weeks (Q2W) by subcutaneous (SC) injection during Week 0 to 16.

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:

Participants received placebo every two weeks (Q2W) by subcutaneous (SC) injection.

Arm title	IXE80Q4W

Arm description:

Participants received starting dose of 80 or 160 mg ixekizumab given SC at baseline followed by 80 mg ixekizumab given SC every four weeks (Q4W) up to week 16.

Arm type	Experimental
Investigational medicinal product name	IXE80Q4W
Investigational medicinal product code	
Other name	LY2439821; Ixekizumab
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

80 or 160 milligrams (mg) of ixekizumab given subcutaneously (SC).

Arm title	IXE80Q2W

Arm description:

Participants received starting dose of 80 or 160 milligrams (mg) ixekizumab given subcutaneously (SC) at baseline followed by 80 mg ixekizumab given SC every two weeks (Q2W) up to week 16.

Arm type	Experimental

Investigational medicinal product name	IXE80Q2W
Investigational medicinal product code	
Other name	LY2439821; Ixekizumab
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

80 or 160 milligrams (mg) of ixekizumab given subcutaneously (SC).

Number of subjects in period 1	Placebo (PBO)	IXE80Q4W	IXE80Q2W
Started	104	114	98
Completed	93	99	90
Not completed	11	15	8
Adverse event, serious fatal	-	-	1
Consent withdrawn by subject	7	3	4
Physician decision	-	1	-
Adverse event, non-fatal	2	9	2
Lost to follow-up	-	1	-
Lack of efficacy	2	1	1

Period 2

Period 2 title	Extended Treatment Period
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	PBO/IXE

Arm description:

Participants who received Placebo in blinded treatment period were re-randomized to receive ixekizumab 80 mg Q4W or 80 mg Q2W at a 1:1 ratio with starting dose of 160 mg.

Arm type	Experimental
Investigational medicinal product name	IXE
Investigational medicinal product code	
Other name	LY2439821; Ixekizumab
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants who received Placebo in blinded treatment period were re- randomized to receive ixekizumab 80 mg Q4W or 80 mg Q2W at a 1:1 ratio with starting dose of 160 mg.

Arm title	IXE80Q4W/IXE80Q4W

Arm description:	
Participants received 80 mg ixekizumab given SC Q4W from week 16 to week 52.	
Arm type	Experimental
Investigational medicinal product name	IXE80Q4W/IXE80Q4W
Investigational medicinal product code	
Other name	LY2439821; Ixekizumab
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Participants received 80 mg ixekizumab given SC Q2W from week 16 to week 52.	
Arm title	IXE80Q2W/IXE80Q2W
Arm description:	
Participants received 80 mg ixekizumab given SC Q2W from week 16 to week 52.	
Arm type	Experimental
Investigational medicinal product name	IXE80Q2W/IXE80Q2W
Investigational medicinal product code	
Other name	LY2439821; Ixekizumab
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Participants received 80 mg ixekizumab given SC Q2W from week 16 to week 52.	

Number of subjects in period 2[1]	PBO/IXE	IXE80Q4W/IXE80Q4W	IXE80Q2W/IXE80Q2W
Started	93	98	90
Completed	81	89	80
Not completed	12	9	10
Consent withdrawn by subject	3	2	3
Physician decision	-	1	-
Adverse event, non-fatal	1	4	5
Lost to follow-up	1	-	-
Lack of efficacy	7	2	2

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: 1 participant completed blinded treatment period and entered post-treatment followup period directly.

Period 3

Period 3 title	Post-treatment 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 did not receive any intervention during Follow-up period	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	IXE80Q4W
Arm description:	
Participants did not receive any intervention during Follow-up period	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	IXE80Q2W
Arm description:	
Participants did not receive any intervention during Follow-up period	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 3[2]	Placebo	IXE80Q4W	IXE80Q2W
Started	5	34	22
Completed	0	8	3
Not completed	5	26	19
Consent withdrawn by subject	2	8	12
Physician decision	-	2	-
Adverse event, non-fatal	2	12	6
No progressive improvement	-	1	-
Lost to follow-up	-	1	1
Lack of efficacy	1	2	-

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Participants who terminate RHBW early or who didn't enroll into RHBY entered Follow-Up Period.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo (PBO)
Reporting group description:	
Participants received placebo every two weeks (Q2W) by subcutaneous (SC) injection during Week 0 to 16.	
Reporting group title	IXE80Q4W
Reporting group description:	
Participants received starting dose of 80 or 160 mg ixekizumab given SC at baseline followed by 80 mg ixekizumab given SC every four weeks (Q4W) up to week 16.	
Reporting group title	IXE80Q2W
Reporting group description:	
Participants received starting dose of 80 or 160 milligrams (mg) ixekizumab given subcutaneously (SC) at baseline followed by 80 mg ixekizumab given SC every two weeks (Q2W) up to week 16.	

Reporting group values	Placebo (PBO)	IXE80Q4W	IXE80Q2W
Number of subjects	104	114	98
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	46.6	47.4	44.2
standard deviation	± 12.72	± 13.36	± 10.79
Gender categorical Units: Subjects			
Female	17	23	23
Male	87	91	75
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	33	32	35
Not Hispanic or Latino	63	70	53
Unknown or Not Reported	8	12	10
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	4	4	4
Asian	13	14	13
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	2	2

White	85	91	78
More than one race	1	2	1
Unknown or Not Reported	0	1	0
Region of Enrollment Units: Subjects			
Puerto Rico	1	2	4
Argentina	6	7	5
United States	14	14	12
United Kingdom	9	6	5
Spain	3	7	4
Canada	1	5	0
South Korea	12	11	11
Netherlands	1	2	0
Finland	0	3	2
Brazil	10	8	10
Poland	22	24	20
Italy	0	1	1
Mexico	13	13	13
Israel	5	5	6
France	7	5	5
Germany	0	1	0

Reporting group values	Total		
Number of subjects	316		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	63		
Male	253		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	100		
Not Hispanic or Latino	186		
Unknown or Not Reported	30		
Race (NIH/OMB) Units: Subjects			

American Indian or Alaska Native	12		
Asian	40		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	5		
White	254		
More than one race	4		
Unknown or Not Reported	1		
Region of Enrollment Units: Subjects			
Puerto Rico	7		
Argentina	18		
United States	40		
United Kingdom	20		
Spain	14		
Canada	6		
South Korea	34		
Netherlands	3		
Finland	5		
Brazil	28		
Poland	66		
Italy	2		
Mexico	39		
Israel	16		
France	17		
Germany	1		

End points

End points reporting groups

Reporting group title	Placebo (PBO)
Reporting group description:	
Participants received placebo every two weeks (Q2W) by subcutaneous (SC) injection during Week 0 to 16.	
Reporting group title	IXE80Q4W
Reporting group description:	
Participants received starting dose of 80 or 160 mg ixekizumab given SC at baseline followed by 80 mg ixekizumab given SC every four weeks (Q4W) up to week 16.	
Reporting group title	IXE80Q2W
Reporting group description:	
Participants received starting dose of 80 or 160 milligrams (mg) ixekizumab given subcutaneously (SC) at baseline followed by 80 mg ixekizumab given SC every two weeks (Q2W) up to week 16.	
Reporting group title	PBO/IXE
Reporting group description:	
Participants who received Placebo in blinded treatment period were re-randomized to receive ixekizumab 80 mg Q4W or 80 mg Q2W at a 1:1 ratio with starting dose of 160 mg.	
Reporting group title	IXE80Q4W/IXE80Q4W
Reporting group description:	
Participants received 80 mg ixekizumab given SC Q4W from week 16 to week 52.	
Reporting group title	IXE80Q2W/IXE80Q2W
Reporting group description:	
Participants received 80 mg ixekizumab given SC Q2W from week 16 to week 52.	
Reporting group title	Placebo
Reporting group description:	
Participants did not receive any intervention during Follow-up period	
Reporting group title	IXE80Q4W
Reporting group description:	
Participants did not receive any intervention during Follow-up period	
Reporting group title	IXE80Q2W
Reporting group description:	
Participants did not receive any intervention during Follow-up period	
Subject analysis set title	Placebo
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received placebo every 2 weeks (Q2W) by subcutaneous injection.	
Subject analysis set title	80 mg Q4W Ixekizumab
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received starting dose of 80 or 160 mg ixekizumab by SC injection at baseline followed by 80 mg ixekizumab given SC every four weeks (Q4W).	
Subject analysis set title	80 mg Q2W Ixekizumab
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received starting dose of 80 or 160 mg ixekizumab given SC injection at baseline followed by 80 mg ixekizumab given SC every two weeks (Q2W) to week 16.	
Subject analysis set title	80 mg Q4W Ixekizumab (Starting Dose 80 mg)
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received 80 mg of Ixekizumab every four weeks by subcutaneous injection.	

Subject analysis set title	80 mg Q4W Ixekizumab (Starting Dose 160 mg)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received 160 mg ixekizumab at baseline followed by 80 mg ixekizumab given SC every four weeks by subcutaneous injection.

Subject analysis set title	80 mg Q2W Ixekizumab (Starting Dose 80 mg)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received 80 mg ixekizumab every two weeks by subcutaneous injection.

Subject analysis set title	80 mg Q2W Ixekizumab (Starting Dose 160 mg)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received starting dose of 160 mg ixekizumab at baseline followed by 80 mg ixekizumab every two weeks by subcutaneous injection.

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 improvement from baseline of >= 40 % and absolute improvement from baseline of at least 2 units in at least 3 of the following 4 domains without any worsening in the remaining domain.
1) Patient Global: How active was your Ankylosing spondylitis (AS) (on average during the last week? score ranges 0 (not active) to 10 (very active).
2) Spinal Pain: How much Pain of your spine due to AS? ranges 0 (no pain) to 10 (severe pain).
3) Bath Ankylosing Spondylitis Functional Index : Participant asked to rate the difficulty associated with 10 individual basic functional activities. Participant response was captured using Numeric Rating Scale (NRS) (range 0 to 10) with a higher score indicating worse function.
4) Inflammation based on Q5 & Q6 mean of Bath Ankylosing Spondylitis Disease Activity Index (mean of intensity & duration of stiffness): Score ranges from "0" (none) and "10" (very severe).
Analysis Population Description (APD): All randomized participants.

End point type	Primary

End point timeframe:

Week 16

End point values	Placebo	80 mg Q4W Ixekizumab	80 mg Q2W Ixekizumab	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	104	114	98	
Units: Percentage of participants				
number (not applicable)	12.5	25.4	30.6	

Statistical analyses

Statistical analysis title	ASAS40 Response
Comparison groups	Placebo v 80 mg Q4W Ixekizumab

Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.017
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.17
upper limit	4.95

Statistical analysis title	ASAS40 Response
Comparison groups	Placebo v 80 mg Q2W Ixekizumab
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.48
upper limit	6.33

Secondary: Percentage of Participants Achieving an ASAS20 Response

End point title	Percentage of Participants Achieving an ASAS20 Response

End point description:

ASAS20 response is defined as a ≥20% improvement and an absolute improvement from baseline of ≥1 units (range 0 to 10) in ≥3 of 4 domains, and no worsening of ≥20% and ≥1 unit (range 0 to 10) in the remaining domain.
1) Patient Global: How active was your spondylitis on average during the last week? score ranges 0 (not active) to 10 (very active).
2) Spinal Pain: How much Pain of your spine due to Ankylosing spondylitis? score ranges 0 (no pain) to 10 (severe pain).
3) Bath Ankylosing Spondylitis Functional Index (BASFI): Participant asked to rate the difficulty associated with 10 individual basic functional activities. Participant response was captured using Numeric Rating Scale (NRS) (range 0 to 10) with a higher score indicating worse function.
4) Inflammation based on Q5 & Q6 mean of Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) (mean of intensity & duration of stiffness): Score ranges from "0" (none) and "10" (very severe).
APD: All randomized participants.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	80 mg Q4W Ixekizumab	80 mg Q2W Ixekizumab	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	104	114	98	
Units: Percentage of Participants				
number (not applicable)	29.8	48.2	46.9	

Statistical analyses

Statistical analysis title	ASAS20 Response
Comparison groups	Placebo v 80 mg Q4W Ixekizumab
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.26
upper limit	3.84

Statistical analysis title	ASAS20 Response
Comparison groups	Placebo v 80 mg Q2W Ixekizumab
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.013
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.16
upper limit	3.73

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 AS. The parameters used for the ASDAS (with CRP as acute phase reactant) are 1) Total back pain, 2) Patient global, 3) Peripheral pain/swelling, 4) Duration of morning stiffness and 5) CRP in mg/L. The 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 mg/liter, the range of other variables is from (0 to 10); Ln represents the natural logarithm). Data from five variables combined to yield a score (0.6361 to no defined upper limit), where higher scores higher disease activity. Least square (LS) mean was determined by mixed-model repeated measures (MMRM) with treatment, geographic region, baseline CRP status, number of prior tumor necrosis factor inhibitor (TNFi), baseline value, visit,baseline value-byvisit,and treatment-by-visit interaction as fixed factors.
APD: All randomized participants.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	80 mg Q4W Ixekizumab	80 mg Q2W Ixekizumab	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	104	114	98	
Units: Units on a scale				
least squares mean (standard error)	-0.11 (± 0.099)	-1.16 (± 0.094)	-1.13 (± 0.103)	

Statistical analyses

Statistical analysis title	ASDAS
Comparison groups	Placebo v 80 mg Q4W Ixekizumab
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.32
upper limit	-0.79
Variability estimate	Standard error of the mean
Dispersion value	0.135

Statistical analysis title	ASDAS
Comparison groups	Placebo v 80 mg Q2W Ixekizumab

Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.75
Variability estimate	Standard error of the mean
Dispersion value	0.14

Secondary: Percentage of Participants Achieving Bath Ankylosing Spondylitis Disease Activity Index 50 (BASDAI50) Response

End point title	Percentage of Participants Achieving Bath Ankylosing Spondylitis Disease Activity Index 50 (BASDAI50) Response

End point description:

The BASDAI is a participant-reported assessment consisting of 6 questions that relate to 5 major symptoms relevant to radiographic axial spondyloarthritis (rad-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. BASDAI50 represents an improvement of ≥50% of the BASDAI score from baseline.
APD: All randomized participants.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	80 mg Q4W Ixekizumab	80 mg Q2W Ixekizumab	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	104	114	98	
Units: Percentage of Participants				
number (not applicable)	9.6	21.9	23.5	

Statistical analyses

Statistical analysis title	BASDAI50
Comparison groups	Placebo v 80 mg Q4W Ixekizumab

Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.21
upper limit	5.84

Statistical analysis title	BASDAI50
Comparison groups	Placebo v 80 mg Q2W Ixekizumab
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.29
upper limit	6.49

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 radiographic axial spondyloarthritis (rad-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. LSmean was determined by MMRM with factors for treatment, geographic region, baseline CRP status, number of prior TNFi, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors.
APD: All randomized participants.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	80 mg Q4W Ixekizumab	80 mg Q2W Ixekizumab	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	104	114	98	
Units: Units on a scale				
least squares mean (standard error)	-0.92 (± 0.212)	-2.17 (± 0.202)	-2.09 (± 0.221)	

Statistical analyses

Statistical analysis title	BASDAI
Comparison groups	Placebo v 80 mg Q4W Ixekizumab
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-1.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.81
upper limit	-0.67
Variability estimate	Standard error of the mean
Dispersion value	0.291

Statistical analysis title	BASDAI
Comparison groups	Placebo v 80 mg Q2W Ixekizumab
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.76
upper limit	-0.57
Variability estimate	Standard error of the mean
Dispersion value	0.301

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:

The BASFI is a participant-reported assessment that establishes a participant's functional baseline and subsequent response to treatment. The BASFI is composed with 10 questions to assess the disease severity, including the first 8 questions regarding to functional anatomy related activities and the remaining 2 questions related to daily activities of AS participants. Participants respond to each question using an NRS scale (range 0 to 10). The BASFI score is the average of the 10 responses and has a possible minimum value of 0 and a possible maximum value of 10, with a higher score indicating worse function. LS mean was determined by MMRM with factors for treatment, geographic region, baseline CRP status, number of prior TNFi, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors.
APD: All randomized participants.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	80 mg Q4W Ixekizumab	80 mg Q2W Ixekizumab	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	104	114	98	
Units: Units on a scale				
least squares mean (standard error)	-0.64 (± 0.215)	-1.69 (± 0.205)	-1.92 (± 0.225)	

Statistical analyses

Statistical analysis title	BASFI
Comparison groups	Placebo v 80 mg Q4W Ixekizumab
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.63
upper limit	-0.47
Variability estimate	Standard error of the mean
Dispersion value	0.295

Statistical analysis title	BASFI
Comparison groups	Placebo v 80 mg Q2W Ixekizumab

Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.89
upper limit	-0.68
Variability estimate	Standard error of the mean
Dispersion value	0.307

Secondary: Percentage of Participants Achieving ASDAS Inactive Disease

End point title	Percentage of Participants Achieving ASDAS Inactive Disease

End point description:

The ASDAS is a self-administered questionnaire/objective laboratory evaluation. The questionnaire assesses disease activity (patient global), back pain, and peripheral pain/swelling on a numeric rating scale (from 0 (normal) to 10 (very severe)) and duration of morning stiffness on a numeric rating scale (from 0 to 10, with 0 being none and 10 representing a duration of ≥2 hours). The laboratory parameter is a measurement of high-sensitivity C-reactive protein (mg/L) (hs-CRP). Data from five variables (disease activity, back pain, duration of morning stiffness, peripheral pain/swelling, and hs-CRP) are combined to yield a score (0.6361 to no defined upper limit), where higher the score worse the disease activity. ASDAS Inactive Disease is defined as a score of <1.3.
APD: All randomized participants.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	80 mg Q4W Ixekizumab	80 mg Q2W Ixekizumab	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	104	114	98	
Units: Percentage of Participants				
number (not applicable)	1.0	3.5	5.1	

Statistical analyses

Statistical analysis title	ASDAS Inactive Disease
Comparison groups	Placebo v 80 mg Q4W Ixekizumab

Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.242
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	33.98

Statistical analysis title	ASDAS Inactive Disease
Comparison groups	Placebo v 80 mg Q2W Ixekizumab
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.127
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	47.54

Secondary: Percentage of Participants Achieving ASDAS <2.1

End point title	Percentage of Participants Achieving ASDAS <2.1

End point description:

The ASDAS is a self-administered questionnaire/objective laboratory evaluation. The questionnaire assesses disease activity (patient global), back pain, and peripheral pain/swelling on a numeric rating scale (from 0 (normal) to 10 (very severe)) and duration of morning stiffness on a numeric rating scale (from 0 to 10, with 0 being none and 10 representing a duration of ≥2 hours). The laboratory parameter is a measurement of high-sensitivity C-reactive protein (mg/L) (hs-CRP). Data from five variables (disease activity, back pain, duration of morning stiffness, peripheral pain/swelling, and hs-CRP) are combined to yield a score (0.6361 to no defined upper limit), where higher the score worse the disease activity. ASDAS <2.1 defines moderate disease activity.
APD: All randomized participants.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	80 mg Q4W Ixekizumab	80 mg Q2W Ixekizumab	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	104	114	98	
Units: Percentage of Participants				
number (not applicable)	4.8	17.5	16.3	

Statistical analyses

Statistical analysis title	ASDAS <2.1
Comparison groups	Placebo v 80 mg Q4W Ixekizumab
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.5
upper limit	11.86

Statistical analysis title	ASDAS <2.1
Comparison groups	Placebo v 80 mg Q2W Ixekizumab
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.55
upper limit	13.18

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

End point title	Change from Baseline in 36-Item Short Form Health Survey (SF-36) Physical Component Summary (PCS) and Mental Component Summary (MCS) Scores

End point description:

The SF-36 is a 36-item participant 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 2 overarching domains of mental well-being and physical well-being are captured by the Mental Component Summary and Physical Component Summary scores. T-scores are used for analysis. The summary scores range from 0 to 100, with higher scores indicating better levels of function and/or better health. LSmean was determined by MMRM with factors for treatment, geographic region, baseline CRP status, number of prior TNFi, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors.
APD: All randomized participants.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	80 mg Q4W Ixekizumab	80 mg Q2W Ixekizumab	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	104	114	98	
Units: Units on a scale				
least squares mean (standard error)				
SF-36 MCS	2.7410 (± 0.9452)	3.5099 (± 0.9074)	3.6514 (± 0.9921)	
SF-36 PCS	1.3638 (± 0.8146)	6.5785 (± 0.7763)	6.1223 (± 0.8465)	

Statistical analyses

Statistical analysis title	SF-36 MCS
Comparison groups	Placebo v 80 mg Q4W Ixekizumab
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.55
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	0.7689
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7629
upper limit	3.3007
Variability estimate	Standard error of the mean
Dispersion value	1.2863

Statistical analysis title	SF-36 MCS
Comparison groups	Placebo v 80 mg Q2W Ixekizumab

Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.495
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	0.9104
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7151
upper limit	3.536
Variability estimate	Standard error of the mean
Dispersion value	1.3338

Statistical analysis title	SF-36 PCS
Comparison groups	Placebo v 80 mg Q4W Ixekizumab
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	5.2147
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.0204
upper limit	7.409
Variability estimate	Standard error of the mean
Dispersion value	1.1149

Statistical analysis title	SF-36 PCS
Comparison groups	Placebo v 80 mg Q2W Ixekizumab
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	4.7585
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.494
upper limit	7.023

Variability estimate	Standard error of the mean
Dispersion value	1.1505

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:

The ASAS Health Index (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 1 question that the patient needs to respond to with either "I agree" (score 1) or "I do not agree (score 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 determined by MMRM with treatment, geographic region, baseline CRP status, number of prior TNFi, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors.
APD: All randomized participants.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	80 mg Q4W Ixekizumab	80 mg Q2W Ixekizumab	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	104	114	98	
Units: Units on a scale				
least squares mean (standard error)	-0.89 (± 0.338)	-1.92 (± 0.322)	-1.58 (± 0.352)	

Statistical analyses

Statistical analysis title	ASAS HI
Comparison groups	Placebo v 80 mg Q4W Ixekizumab
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.026
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.94
upper limit	-0.13
Variability estimate	Standard error of the mean
Dispersion value	0.46

Statistical analysis title	ASAS HI
Comparison groups	Placebo v 80 mg Q2W Ixekizumab
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.149
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.63
upper limit	0.25
Variability estimate	Standard error of the mean
Dispersion value	0.477

Secondary: Change from Baseline in Magnetic Resonance Imaging (MRI) of the Spine (Ankylosing Spondylitis Spinal Magnetic Resonance Imaging [ASSpiMRI] – Berlin Score)

End point title	Change from Baseline in Magnetic Resonance Imaging (MRI) of the Spine (Ankylosing Spondylitis Spinal Magnetic Resonance Imaging [ASSpiMRI] – Berlin Score)

End point description:

The study used MRI with fat-saturating techniques such as short tau inversion recovery (STIR) to look for the presence of bone marrow edema. The Berlin modification of Ankylosing Spondylitis spine MRI score for activity (ASspiMRI) scoring technique assesses inflammation in each of the 23 disco-vertebral units (DVU) of the spine (from C2 to S1), capturing bone marrow edema. Scores for each DVU range from 0-3 (0=normal; 1=minor bone marrow edema [less than or equal to 25% of DVU; 3=severe bone marrow edema (more that 50% of DVU)]. The composite score ranges from 0 to 69, with higher scores reflecting worse disease.LS mean was determined by analysis of covariance (ANCOVA) with treatment, geographic region, baseline CRP status, number of prior TNF inhibitors used and baseline value as fixed factors.
APD: All randomized participants with baseline and week 16 ASSpiMRI score.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	80 mg Q4W Ixekizumab	80 mg Q2W Ixekizumab	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	46	49	45	
Units: Units on a scale				
least squares mean (standard error)	1.03 (± 0.379)	-0.92 (± 0.373)	-1.14 (± 0.414)	

Statistical analyses

Statistical analysis title	ASSpiMRI score
Comparison groups	Placebo v 80 mg Q4W Ixekizumab
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-1.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	-0.9
Variability estimate	Standard error of the mean
Dispersion value	0.512

Statistical analysis title	ASSpiMRI score
Comparison groups	Placebo v 80 mg Q2W Ixekizumab
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-2.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.2
upper limit	-1.1
Variability estimate	Standard error of the mean
Dispersion value	0.534

Secondary: Change from Baseline in Magnetic Resonance Imaging (MRI) of the Spine (Spondyloarthritis Research Consortium of Canada [SPARCC] score)

End point title	Change from Baseline in Magnetic Resonance Imaging (MRI) of the Spine (Spondyloarthritis Research Consortium of Canada [SPARCC] score)

End point description:

MRI score of spine was assessed using SPARCC method. All 23 disco-vertebral units (DVU) of the spine (from C2 to S1) were scored for bone marrow edema. A single DVU has 18 scoring units, and each has score of 0 or 1, bringing the maximum total score to 414, the sum ranges from 0 to 414 with higher scores reflecting worse disease. Scoring was performed by central readers. LS mean was determined by ANCOVA with factors for treatment, geographic region, baseline CRP status, number of prior TNF inhibitors used and baseline value.
APD: All randomized participants with baseline and week 16 SPARCC MRI score.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	80 mg Q4W Ixekizumab	80 mg Q2W Ixekizumab	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	46	49	45	
Units: Units on a scale				
least squares mean (standard error)	3.29 (± 1.402)	-2.99 (± 1.384)	-3.97 (± 1.534)	

Statistical analyses

Statistical analysis title	SPARCC score
Comparison groups	Placebo v 80 mg Q4W Ixekizumab
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-6.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10
upper limit	-2.5
Variability estimate	Standard error of the mean
Dispersion value	1.896

Statistical analysis title	SPARCC score
Comparison groups	Placebo v 80 mg Q2W Ixekizumab

Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-7.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.2
upper limit	-3.4
Variability estimate	Standard error of the mean
Dispersion value	1.978

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 CRP is the measure of acute phase reactant. It was measured with a high sensitivity assay at the central laboratory to help assess the effect of ixekizumab on disease activity. High sensitivity CRP is a sensitive laboratory assay for serum levels of C-Reactive Protein, which is a biomarker of inflammation. LS mean was determined by MMRM with treatment, geographic region, baseline CRP status, number of prior TNFi, visit, and treatment-by-visit interaction as fixed factors. APD: All randomized participants.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	80 mg Q4W Ixekizumab	80 mg Q2W Ixekizumab	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	104	114	98	
Units: milligram per liter (mg/L)				
least squares mean (standard error)	9.719 (± 2.7383)	-11.096 (± 2.6190)	-8.121 (± 2.8829)	

Statistical analyses

Statistical analysis title	High Sensitivity C-Reactive Protein
Comparison groups	Placebo v 80 mg Q4W Ixekizumab

Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-20.816
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.187
upper limit	-13.444
Variability estimate	Standard error of the mean
Dispersion value	3.7463

Statistical analysis title	High Sensitivity C-Reactive Protein
Comparison groups	Placebo v 80 mg Q2W Ixekizumab
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-17.841
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.518
upper limit	-10.163
Variability estimate	Standard error of the mean
Dispersion value	3.9018

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:

BASMI is a combined index comprising of 5 clinical measurements of spinal mobility in patients with radaxSpA.
1) Lateral Spinal Flexion
2) Tragus-to-wall distance
3) Lumbar Flexion (modified Schober)
4) Maximal intermalleolar distance and
5) Cervical rotation. The BASMI linear result is the average of the 5 assessments and ranges from 0 to 10. The higher the BASMI score the more severe the patient’s limitation of movement due to their AS.
LS mean was determined by MMRM with treatment, geographic region, baseline CRP status, number of prior TNFi, baseline value, visit, baseline value-by-visit and treatment-by-visit interaction as fixed factors.
APD: All randomized participants.

End point type	Secondary

End point timeframe:
Baseline, Week 16

End point values	Placebo	80 mg Q4W Ixekizumab	80 mg Q2W Ixekizumab	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	104	114	98	
Units: Units on a scale				
least squares mean (standard error)	-0.046 (± 0.0939)	-0.349 (± 0.0897)	-0.217 (± 0.0981)	

Statistical analyses

Statistical analysis title	BASMI
Comparison groups	Placebo v 80 mg Q4W Ixekizumab
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.018
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-0.304
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.555
upper limit	-0.053
Variability estimate	Standard error of the mean
Dispersion value	0.1275

Statistical analysis title	BASMI
Comparison groups	Placebo v 80 mg Q2W Ixekizumab
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.194
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-0.172
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.431
upper limit	0.088

Variability estimate	Standard error of the mean
Dispersion value	0.1319

Secondary: Change from Baseline in Chest Expansion

End point title	Change from Baseline in Chest Expansion

End point description:

Chest expansion is the difference, in centimeter (cm), between the circumference of the chest in maximal inspiration and maximal expiration. While patients have their hands resting on or behind the head, the assessor will measure the chest encircled length by centimeter (cm) at the fourth intercostal level anteriorly. Two tries were recorded. The better measurement (larger difference) of 2 tries (in centimeters) was used for analyses. LS mean was determined by MMRM with treatment, geographic region, baseline CRP status, number of prior TNFi, baseline value, visit, baseline value-by-visit and treatment-by-visit interaction as fixed factors.
APD: All randomized participants.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	80 mg Q4W Ixekizumab	80 mg Q2W Ixekizumab	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	104	114	98	
Units: centimeter(cm)				
least squares mean (standard error)	0.04 (± 0.644)	1.27 (± 0.618)	0.27 (± 0.655)	

Statistical analyses

Statistical analysis title	Chest Expansion
Comparison groups	Placebo v 80 mg Q4W Ixekizumab
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.17
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.53
upper limit	2.99
Variability estimate	Standard error of the mean
Dispersion value	0.893

Statistical analysis title	Chest Expansion
Comparison groups	Placebo v 80 mg Q2W Ixekizumab
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.57
upper limit	2.04
Variability estimate	Standard error of the mean
Dispersion value	0.916

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 determined by MMRM with factors for treatment, geographic region, baseline CRP status, number of prior TNFi, baseline value, visit, baseline value-by-visit and treatment-by-visit interaction as fixed factors.
APD: All randomized participants.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	80 mg Q4W Ixekizumab	80 mg Q2W Ixekizumab	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	104	114	98	
Units: cm				
least squares mean (standard error)	0.35 (± 0.384)	0.03 (± 0.365)	-0.65 (± 0.399)	

Statistical analyses

Statistical analysis title	Occiput to Wall Distance
Comparison groups	Placebo v 80 mg Q4W Ixekizumab

Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.547
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.34
upper limit	0.71
Variability estimate	Standard error of the mean
Dispersion value	0.521

Statistical analysis title	Occiput to Wall Distance
Comparison groups	Placebo v 80 mg Q2W Ixekizumab
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.064
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.06
upper limit	0.06
Variability estimate	Standard error of the mean
Dispersion value	0.538

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:

The 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 include costochondral 1 (right/left), costochondral 7 (right/left), spinal iliaca anterior superior (right/left), crista iliaca (right/left), spina iliaca posterior (right/left), processus spinosus L5, and Achilles tendon proximal insertion (right/left). The MASES is the sum of all site scores (range 0 to 13); higher scores indicate more severe enthesitis. LS mean was determined by MMRM with treatment, geographic region, baseline CRP status, number of prior TNFi, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors.
APD: All randomized participants with baseline MASES score>0.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	80 mg Q4W Ixekizumab	80 mg Q2W Ixekizumab	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	69	82	74	
Units: Units on a scale				
least squares mean (standard error)	-1.9 (± 0.43)	-1.8 (± 0.40)	-2.2 (± 0.42)	

Statistical analyses

Statistical analysis title	MASES
Comparison groups	Placebo v 80 mg Q4W Ixekizumab
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.861
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1.3
Variability estimate	Standard error of the mean
Dispersion value	0.58

Statistical analysis title	MASES
Comparison groups	Placebo v 80 mg Q2W Ixekizumab
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.626
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.59

Secondary: Change from Baseline in Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Score

End point title	Change from Baseline in Spondyloarthritis Research Consortium of Canada (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 determined by MMRM with treatment, geographic region, baseline CRP status, number of prior TNFi, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors.
APD: All randomized participants with baseline SPARCC Enthesitis score>0.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	80 mg Q4W Ixekizumab	80 mg Q2W Ixekizumab	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	60	78	64	
Units: Units on a scale				
least squares mean (standard error)	-1.9 (± 0.44)	-2.3 (± 0.40)	-1.8 (± 0.45)	

Statistical analyses

Statistical analysis title	SPARCC- Enthesitis Score
Comparison groups	Placebo v 80 mg Q4W Ixekizumab
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.504
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.59

Statistical analysis title	SPARCC- Enthesitis Score
Comparison groups	Placebo v 80 mg Q2W Ixekizumab
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.86
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.3
Variability estimate	Standard error of the mean
Dispersion value	0.62

Secondary: Change from Baseline in Severity of Peripheral Arthritis by Tender Joint Count (TJC) Scores

End point title	Change from Baseline in Severity of Peripheral Arthritis by Tender Joint Count (TJC) Scores

End point description:

The number of tender and painful joints was determined by examination of 46 joints (23 joints on each side of the body). The 46 joints were assessed and classified as tender or not tender. Sum of all joints checked to be tender/painful divided by number of evaluable joints which was multiplied by 46 to obtain TJC score. The scores ranges from 0 (no tender/painful joints) to 46 (all joints tender/painful). LS mean was determined by MMRM with treatment, geographic region, baseline CRP status, number of prior TNFi, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction.
APD: All randomized participants with baseline TJC>0.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	80 mg Q4W Ixekizumab	80 mg Q2W Ixekizumab	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	65	85	69	
Units: Tender Joint Count				
least squares mean (standard error)	-3.9 (± 0.79)	-4.8 (± 0.69)	-5.0 (± 0.79)	

Statistical analyses

Statistical analysis title	TJC Scores
Comparison groups	Placebo v 80 mg Q4W Ixekizumab
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.362
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	1.03

Statistical analysis title	TJC Scores
Comparison groups	Placebo v 80 mg Q2W Ixekizumab
Number of subjects included in analysis	134
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.303
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	1.08

Secondary: Change from Baseline in Severity of Peripheral Arthritis by Swollen Joint Count (SJC) Scores

End point title	Change from Baseline in Severity of Peripheral Arthritis by Swollen Joint Count (SJC) Scores

End point description:

The number of swollen joints was determined by examination of 44 joints (22 joints on each side of the body). The 44 joints were assessed and classified as swollen or not swollen. Sum of all joints checked to be swollen divided by number of evaluable joints which was multiplied by 44 to obtain SJC score. The SJC score ranges from 0 (no swollen joints) to 44 (all joints swollen). LS mean was determined by MMRM with treatment, geographic region, baseline CRP status, number of prior TNFi, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction.
APD: All randomized participants with baseline SJC>0.

End point type	Secondary

End point timeframe:
Baseline, Week 16

End point values	Placebo	80 mg Q4W Ixekizumab	80 mg Q2W Ixekizumab	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	45	48	44	
Units: Swollen Joint Count				
least squares mean (standard error)	-2.4 (± 0.51)	-2.6 (± 0.49)	-3.0 (± 0.54)	

Statistical analyses

Statistical analysis title	SJC Scores
Comparison groups	Placebo v 80 mg Q4W Ixekizumab
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.813
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	1.2
Variability estimate	Standard error of the mean
Dispersion value	0.7

Statistical analysis title	SJC Scores
Comparison groups	Placebo v 80 mg Q2W Ixekizumab
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.41
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	0.8

Variability estimate	Standard error of the mean
Dispersion value	0.71

Secondary: Percentage of Participants with Anterior Uveitis

End point title	Percentage of Participants with Anterior Uveitis

End point description:

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.
APD: All randomized participants.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	80 mg Q4W Ixekizumab	80 mg Q2W Ixekizumab	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	104	114	98	
Units: Percentage of Participants				
number (not applicable)	0	1.8	3.1	

Statistical analyses

Statistical analysis title	Anterior Uveitis
Comparison groups	Placebo v 80 mg Q4W Ixekizumab
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.499
Method	Fisher exact
Parameter estimate	Incidence Rate
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	4.2

Statistical analysis title	Anterior Uveitis
Comparison groups	Placebo v 80 mg Q2W Ixekizumab

Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.112
Method	Fisher exact
Parameter estimate	Incidence Rate
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	6.5

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 1 number that describes their worst level of fatigue during the previous 24 hours. LS mean was determined by MMRM with treatment, geographic region, baseline CRP status, number of prior TNFi, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors.
APD: All randomized participants.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	80 mg Q4W Ixekizumab	80 mg Q2W Ixekizumab	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	104	114	98	
Units: Units on a scale				
least squares mean (standard error)	-0.7 (± 0.24)	-2.0 (± 0.23)	-1.7 (± 0.25)	

Statistical analyses

Statistical analysis title	Fatigue NRS Score
Comparison groups	Placebo v 80 mg Q4W Ixekizumab
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-1.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	-0.6
Variability estimate	Standard error of the mean
Dispersion value	0.33

Statistical analysis title	Fatigue NRS Score
Comparison groups	80 mg Q2W Ixekizumab v Placebo
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	-0.3
Variability estimate	Standard error of the mean
Dispersion value	0.34

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:

The 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 determined by MMRM with treatment, geographic region, baseline CRP status, number of prior TNFi, baseline value, visit, baseline value-by-visit and treatment-by-visit interaction as fixed factors.
APD: All randomized participants.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	80 mg Q4W Ixekizumab	80 mg Q2W Ixekizumab	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	104	114	98	
Units: Units on a scale				
least squares mean (standard error)	-1.8 (± 0.50)	-3.0 (± 0.48)	-2.4 (± 0.52)	

Statistical analyses

Statistical analysis title	JSEQ
Comparison groups	Placebo v 80 mg Q4W Ixekizumab
Number of subjects included in analysis	218
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.088
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.68

Statistical analysis title	JSEQ
Comparison groups	Placebo v 80 mg Q2W Ixekizumab
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.366
Method	Mixed models analysis
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.7

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 determined by ANCOVA with treatment, geographic region, baseline CRP status, number of prior TNFi and baseline value as fixed factors.
APD: All randomized participants with baseline and week 16 WPAI-SpA score.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo	80 mg Q4W Ixekizumab	80 mg Q2W Ixekizumab	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	99[1]	112[2]	96[3]	
Units: Units on a scale				
least squares mean (standard error)				
Overall Work Impairment Score	-9.84 (± 3.733)	-20.97 (± 4.016)	-23.50 (± 4.225)	
Percentage of Activity Impairment	-10.1 (± 2.60)	-16.5 (± 2.44)	-18.4 (± 2.74)	

Notes:

[1] - N=54 for Overall Work Impairment Score

[2] - N= 44 for Overall Work Impairment Score

[3] - N= 43 for Overall Work Impairment Score

Statistical analyses

Statistical analysis title	Overall Work Impairment Score

Statistical analysis description:

Subjects in this analysis: 98

Comparison groups	Placebo v 80 mg Q4W Ixekizumab
Number of subjects included in analysis	211
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.038
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-11.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.65
upper limit	-0.6
Variability estimate	Standard error of the mean
Dispersion value	5.323

Statistical analysis title	Overall Work Impairment Score
Statistical analysis description: Subjects in this analysis: 97	
Comparison groups	Placebo v 80 mg Q2W Ixekizumab
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-13.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.23
upper limit	-3.1
Variability estimate	Standard error of the mean
Dispersion value	5.341

Statistical analysis title	Percentage of Activity Impairment
Comparison groups	Placebo v 80 mg Q4W Ixekizumab
Number of subjects included in analysis	211
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.071
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-6.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.2
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	3.5

Statistical analysis title	Percentage of Activity Impairment
Comparison groups	Placebo v 80 mg Q2W Ixekizumab

Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.024
Method	ANCOVA
Parameter estimate	LS Mean Difference (Final Values)
Point estimate	-8.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.5
upper limit	-1.1
Variability estimate	Standard error of the mean
Dispersion value	3.65

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, higher the score greated the NSAID intake. ASAS-NSAID score= (equivalent NSAID score) x (days of intake during PI) x (days per week)/(PI in days).
APD: Participants from extended treatment period who had NSAID Intake at baseline.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	PBO/IXE	IXE80Q4W/IXE 80Q4W	IXE80Q2W/IXE 80Q2W	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69	71	58	
Units: Units on a scale				
arithmetic mean (standard deviation)	-9.84 (± 34.435)	-5.52 (± 19.553)	-2.33 (± 24.019)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Anti-Ixekizumab Antibodies

End point title	Percentage of Participants with Anti-Ixekizumab Antibodies

End point description:

A TE-ADA positive patient is defined as: a) a patient with a >= 4-fold increase over a positive baseline antibody titer; or b) for a negative baseline titer, a patient with an increase from the baseline to a level

of >= 1:10. Percentage of participants with treatment-emergent positive anti-ixekizumab antibodies was summarized by treatment group. Percentage was calculated based on the number of evaluable participants and was calculated by number of participants with treatment-emergent positive anti-ixekizumab antibodies / number of evaluable participants * 100%.
APD: All randomized participants.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo	80 mg Q4W Ixekizumab	80 mg Q2W Ixekizumab	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	104	113	98	
Units: Percentage of Participants				
number (not applicable)	2.9	7.1	4.1	

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Trough Ixekizumab Concentration at Steady State (Ctrough ss)

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

End point description:

Pharmacokinetics (PK): Steady-state trough serum concentration of Ixekizumab at week 16.
APD: All randomized participants who received study drug and have evaluable PK data.

End point type	Secondary

End point timeframe:

Predose, Week 1, 2, 4, 8, 12 and Week 16

End point values	80 mg Q4W Ixekizumab (Starting Dose 80 mg)	80 mg Q4W Ixekizumab (Starting Dose 160 mg)	80 mg Q2W Ixekizumab (Starting Dose 80 mg)	80 mg Q2W Ixekizumab (Starting Dose 160 mg)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	60	54	48	50
Units: Microgram/milliliters (µg/mL)				
geometric mean (geometric coefficient of variation)				
Week 16	2.10 (± 106)	2.47 (± 101)	6.27 (± 158)	8.52 (± 50)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Blinded Treatment, Extended Treatment and Follow-Up Periods	
Adverse event reporting additional description:	
I1F-MC-RHBW	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	IXE80Q2W-blinded treatment period
Reporting group description: -	
Reporting group title	IXE80Q4W-blinded treatment period
Reporting group description: -	
Reporting group title	PBO-blinded treatment period
Reporting group description: -	
Reporting group title	IXE80Q2W/IXE80Q2W-extended treatment period
Reporting group description: -	
Reporting group title	IXE80Q4W/IXE80Q4W-extended treatment period
Reporting group description: -	
Reporting group title	IXE80Q2W-follow-up period
Reporting group description: -	
Reporting group title	PBO/IXE-extended treatment period
Reporting group description: -	
Reporting group title	IXE80Q4W-follow-up period
Reporting group description: -	
Reporting group title	PBO-follow-up period
Reporting group description: -	

Serious adverse events	IXE80Q2W-blinded treatment period	IXE80Q4W-blinded treatment period	PBO-blinded treatment period
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 98 (3.06%)	4 / 114 (3.51%)	5 / 104 (4.81%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
acute promyelocytic leukaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 98 (0.00%)	0 / 114 (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

lung adenocarcinoma			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 98 (0.00%)	0 / 114 (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
Vascular disorders			
vasculitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 98 (0.00%)	0 / 114 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
dyspnoea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 98 (0.00%)	0 / 114 (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
pulmonary embolism			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 98 (0.00%)	0 / 114 (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
Psychiatric disorders			
completed suicide			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 114 (0.00%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
depression			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 114 (0.00%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			

blood creatine phosphokinase increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 114 (0.00%)	0 / 104 (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
Injury, poisoning and procedural complications			
femur fracture			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 98 (0.00%)	0 / 114 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
acute myocardial infarction			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 98 (0.00%)	0 / 114 (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
atrial tachycardia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 114 (0.00%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
bradycardia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 98 (0.00%)	0 / 114 (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
Nervous system disorders			
drop attacks			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 98 (0.00%)	0 / 114 (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

loss of consciousness			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 98 (0.00%)	0 / 114 (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
meralgia paraesthetica			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 98 (0.00%)	0 / 114 (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
syncope			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 98 (0.00%)	0 / 114 (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
Gastrointestinal disorders			
colitis ulcerative			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 98 (0.00%)	0 / 114 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
crohn's disease			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 98 (0.00%)	1 / 114 (0.88%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
inguinal hernia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 98 (0.00%)	0 / 114 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 98 (0.00%)	0 / 114 (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
urinary retention			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 98 (0.00%)	0 / 114 (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			
arthritis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 98 (0.00%)	0 / 114 (0.00%)	1 / 104 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
fracture pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 98 (0.00%)	1 / 114 (0.88%)	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
osteoarthritis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 98 (0.00%)	0 / 114 (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			
gastroenteritis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 98 (0.00%)	0 / 114 (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
peritonitis			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 98 (0.00%)	1 / 114 (0.88%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pharyngitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 98 (0.00%)	1 / 114 (0.88%)	0 / 104 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 98 (0.00%)	0 / 114 (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
sinusitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 98 (0.00%)	0 / 114 (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
Metabolism and nutrition disorders			
hyperkalaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 98 (0.00%)	0 / 114 (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/IXE80Q2W-extended treatment period	IXE80Q4W/IXE80Q4W-extended treatment period	IXE80Q2W-follow-up period
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 90 (1.11%)	2 / 98 (2.04%)	1 / 22 (4.55%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
acute promyelocytic leukaemia			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 90 (0.00%)	0 / 98 (0.00%)	0 / 22 (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
lung adenocarcinoma			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 90 (0.00%)	0 / 98 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
vasculitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 90 (0.00%)	0 / 98 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
dyspnoea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 90 (0.00%)	0 / 98 (0.00%)	0 / 22 (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
pulmonary embolism			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 90 (0.00%)	0 / 98 (0.00%)	0 / 22 (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			
completed suicide			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 90 (0.00%)	0 / 98 (0.00%)	0 / 22 (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
depression			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 90 (0.00%)	0 / 98 (0.00%)	0 / 22 (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
Investigations			
blood creatine phosphokinase increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 90 (0.00%)	0 / 98 (0.00%)	0 / 22 (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
Injury, poisoning and procedural complications			
femur fracture			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 90 (0.00%)	0 / 98 (0.00%)	0 / 22 (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
Cardiac disorders			
acute myocardial infarction			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 90 (0.00%)	0 / 98 (0.00%)	0 / 22 (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
atrial tachycardia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 90 (0.00%)	0 / 98 (0.00%)	0 / 22 (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
bradycardia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 90 (0.00%)	1 / 98 (1.02%)	0 / 22 (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
Nervous system disorders			
drop attacks			

alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 90 (0.00%)	0 / 98 (0.00%)	0 / 22 (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
loss of consciousness			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 90 (0.00%)	0 / 98 (0.00%)	0 / 22 (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
meralgia paraesthetica			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 90 (0.00%)	0 / 98 (0.00%)	0 / 22 (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
syncope			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 90 (0.00%)	0 / 98 (0.00%)	0 / 22 (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			
colitis ulcerative			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 90 (0.00%)	0 / 98 (0.00%)	0 / 22 (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
crohn's disease			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 90 (0.00%)	0 / 98 (0.00%)	0 / 22 (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
inguinal hernia			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 90 (0.00%)	0 / 98 (0.00%)	0 / 22 (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
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 90 (0.00%)	1 / 98 (1.02%)	0 / 22 (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
urinary retention			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 90 (0.00%)	1 / 98 (1.02%)	0 / 22 (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
Musculoskeletal and connective tissue disorders			
arthritis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 90 (0.00%)	0 / 98 (0.00%)	0 / 22 (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
fracture pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 90 (0.00%)	0 / 98 (0.00%)	0 / 22 (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 / 90 (0.00%)	0 / 98 (0.00%)	0 / 22 (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			
gastroenteritis			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	1 / 90 (1.11%)	0 / 98 (0.00%)	0 / 22 (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
peritonitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 90 (0.00%)	0 / 98 (0.00%)	0 / 22 (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
pharyngitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 90 (0.00%)	0 / 98 (0.00%)	0 / 22 (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
pneumonia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 90 (0.00%)	0 / 98 (0.00%)	0 / 22 (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 / 90 (0.00%)	0 / 98 (0.00%)	0 / 22 (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
Metabolism and nutrition disorders			
hyperkalaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 90 (0.00%)	1 / 98 (1.02%)	0 / 22 (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

Serious adverse events	PBO/IXE-extended treatment period	IXE80Q4W-follow-up period	PBO-follow-up period
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 93 (6.45%)	2 / 34 (5.88%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0

number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
acute promyelocytic leukaemia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 93 (0.00%)	1 / 34 (2.94%)	0 / 5 (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
lung adenocarcinoma			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 93 (0.00%)	0 / 34 (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
Vascular disorders			
vasculitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 93 (0.00%)	0 / 34 (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
Respiratory, thoracic and mediastinal disorders			
dyspnoea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 93 (1.08%)	0 / 34 (0.00%)	0 / 5 (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
pulmonary embolism			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 93 (0.00%)	1 / 34 (2.94%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
completed suicide			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 93 (0.00%)	0 / 34 (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
depression			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 93 (0.00%)	0 / 34 (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
Investigations			
blood creatine phosphokinase increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 93 (0.00%)	0 / 34 (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
Injury, poisoning and procedural complications			
femur fracture			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 93 (0.00%)	0 / 34 (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
Cardiac disorders			
acute myocardial infarction			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 93 (1.08%)	0 / 34 (0.00%)	0 / 5 (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
atrial tachycardia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 93 (0.00%)	0 / 34 (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
bradycardia			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	1 / 93 (1.08%)	0 / 34 (0.00%)	0 / 5 (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
Nervous system disorders			
drop attacks			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 93 (1.08%)	0 / 34 (0.00%)	0 / 5 (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
loss of consciousness			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 93 (0.00%)	1 / 34 (2.94%)	0 / 5 (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
meralgia paraesthetica			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 93 (1.08%)	0 / 34 (0.00%)	0 / 5 (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
syncope			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 93 (0.00%)	1 / 34 (2.94%)	0 / 5 (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
Gastrointestinal disorders			
colitis ulcerative			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 93 (0.00%)	0 / 34 (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
crohn's disease			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 93 (0.00%)	0 / 34 (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
inguinal hernia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 93 (1.08%)	0 / 34 (0.00%)	0 / 5 (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
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 93 (0.00%)	0 / 34 (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
urinary retention			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 93 (0.00%)	0 / 34 (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			
arthritis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 93 (0.00%)	0 / 34 (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
fracture pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 93 (0.00%)	0 / 34 (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	1 / 93 (1.08%)	0 / 34 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
gastroenteritis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 93 (0.00%)	0 / 34 (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
peritonitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 93 (0.00%)	0 / 34 (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
pharyngitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 93 (0.00%)	0 / 34 (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
pneumonia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 93 (1.08%)	0 / 34 (0.00%)	0 / 5 (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
sinusitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 93 (1.08%)	0 / 34 (0.00%)	0 / 5 (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
Metabolism and nutrition disorders			
hyperkalaemia			
alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	0 / 93 (0.00%)	0 / 34 (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

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

Non-serious adverse events	IXE80Q2W-blinded treatment period	IXE80Q4W-blinded treatment period	PBO-blinded treatment period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 98 (25.51%)	25 / 114 (21.93%)	12 / 104 (11.54%)
Investigations			
blood triglycerides increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 98 (0.00%)	0 / 114 (0.00%)	1 / 104 (0.96%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
injection site reaction			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	8 / 98 (8.16%)	3 / 114 (2.63%)	1 / 104 (0.96%)
occurrences (all)	21	5	1
Gastrointestinal disorders			
diarrhoea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	4 / 98 (4.08%)	6 / 114 (5.26%)	0 / 104 (0.00%)
occurrences (all)	4	6	0
Reproductive system and breast disorders			
vulvovaginal burning sensation			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed[1]	0 / 23 (0.00%)	0 / 23 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
vulvovaginal dryness			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed[2]	0 / 23 (0.00%)	0 / 23 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

arthralgia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 98 (3.06%)	7 / 114 (6.14%)	4 / 104 (3.85%)
occurrences (all)	3	8	4
back pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 98 (3.06%)	1 / 114 (0.88%)	2 / 104 (1.92%)
occurrences (all)	3	1	2
Infections and infestations			
nasopharyngitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	4 / 98 (4.08%)	5 / 114 (4.39%)	2 / 104 (1.92%)
occurrences (all)	4	5	2
upper respiratory tract infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	4 / 98 (4.08%)	9 / 114 (7.89%)	3 / 104 (2.88%)
occurrences (all)	4	12	3
urinary tract infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 98 (2.04%)	0 / 114 (0.00%)	0 / 104 (0.00%)
occurrences (all)	2	0	0
vulvovaginal candidiasis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed[3]	0 / 23 (0.00%)	0 / 23 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	IXE80Q2W/IXE80Q2W-extended treatment period	IXE80Q4W/IXE80Q4W-extended treatment period	IXE80Q2W-follow-up period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 90 (28.89%)	19 / 98 (19.39%)	1 / 22 (4.55%)
Investigations			
blood triglycerides increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 90 (1.11%)	0 / 98 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			

injection site reaction alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all)	5 / 90 (5.56%) 14	2 / 98 (2.04%) 2	0 / 22 (0.00%) 0
Gastrointestinal disorders diarrhoea alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all)	2 / 90 (2.22%) 2	1 / 98 (1.02%) 1	0 / 22 (0.00%) 0
Reproductive system and breast disorders vulvovaginal burning sensation alternative dictionary used: MedDRA 22.0 subjects affected / exposed[1] occurrences (all)	0 / 22 (0.00%) 0	1 / 17 (5.88%) 1	0 / 4 (0.00%) 0
vulvovaginal dryness alternative dictionary used: MedDRA 22.0 subjects affected / exposed[2] occurrences (all)	0 / 22 (0.00%) 0	1 / 17 (5.88%) 1	0 / 4 (0.00%) 0
Musculoskeletal and connective tissue disorders arthralgia alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all)	2 / 90 (2.22%) 2	4 / 98 (4.08%) 4	1 / 22 (4.55%) 2
back pain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all)	5 / 90 (5.56%) 5	6 / 98 (6.12%) 8	0 / 22 (0.00%) 0
Infections and infestations nasopharyngitis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all)	4 / 90 (4.44%) 4	3 / 98 (3.06%) 3	0 / 22 (0.00%) 0
upper respiratory tract infection alternative dictionary used: MedDRA 22.0			

subjects affected / exposed	8 / 90 (8.89%)	4 / 98 (4.08%)	0 / 22 (0.00%)
occurrences (all)	10	4	0
urinary tract infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	5 / 90 (5.56%)	2 / 98 (2.04%)	0 / 22 (0.00%)
occurrences (all)	5	2	0
vulvovaginal candidiasis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed[3]	0 / 22 (0.00%)	0 / 17 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	PBO/IXE-extended treatment period	IXE80Q4W-follow-up period	PBO-follow-up period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 93 (20.43%)	3 / 34 (8.82%)	1 / 5 (20.00%)
Investigations			
blood triglycerides increased			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	1 / 93 (1.08%)	0 / 34 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
injection site reaction			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 93 (3.23%)	0 / 34 (0.00%)	0 / 5 (0.00%)
occurrences (all)	9	0	0
Gastrointestinal disorders			
diarrhoea			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 93 (3.23%)	0 / 34 (0.00%)	0 / 5 (0.00%)
occurrences (all)	3	0	0
Reproductive system and breast disorders			
vulvovaginal burning sensation			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed[1]	0 / 16 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
vulvovaginal dryness			

alternative dictionary used: MedDRA 22.0			
subjects affected / exposed[2]	0 / 16 (0.00%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	4 / 93 (4.30%)	1 / 34 (2.94%)	0 / 5 (0.00%)
occurrences (all)	5	1	0
back pain			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	0 / 93 (0.00%)	0 / 34 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
nasopharyngitis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	3 / 93 (3.23%)	2 / 34 (5.88%)	0 / 5 (0.00%)
occurrences (all)	3	2	0
upper respiratory tract infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	5 / 93 (5.38%)	0 / 34 (0.00%)	0 / 5 (0.00%)
occurrences (all)	5	0	0
urinary tract infection			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed	2 / 93 (2.15%)	0 / 34 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
vulvovaginal candidiasis			
alternative dictionary used: MedDRA 22.0			
subjects affected / exposed[3]	1 / 16 (6.25%)	0 / 9 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	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 or female participants. The number of participants 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 or female participants. The number of participants exposed has been adjusted accordingly.

[3] - 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 or female participants. The number of participants exposed has been adjusted accordingly.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported