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

Summary

EudraCT number	2015-003932-11
Trial protocol	DE HU PL NL CZ
Global end of trial date	17 October 2018

Results information

Result version number	v2 (current)
This version publication date	29 December 2019
First version publication date	10 October 2019
Version creation reason	• Correction of full data set Correction of full data set

Trial information

Trial identification

Sponsor protocol code	I1F-MC-RHBV

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02696785
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 16178

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	17 October 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 October 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study is to evaluate the safety and efficacy of the study drug known as ixekizumab in biological disease-modifying anti-rheumatic drugs (bDMARDs)-naive 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	02 May 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	Korea, Republic of: 47
Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	United States: 15
Country: Number of subjects enrolled	Japan: 7
Country: Number of subjects enrolled	Taiwan: 51
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Canada: 9
Country: Number of subjects enrolled	Hungary: 10
Country: Number of subjects enrolled	Mexico: 30
Country: Number of subjects enrolled	Poland: 62
Country: Number of subjects enrolled	Russian Federation: 48
Country: Number of subjects enrolled	Czech Republic: 54
Worldwide total number of subjects	340
EEA total number of subjects	133

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)	326
From 65 to 84 years	14
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Blinded treatment period (Week 0 to Week 16), followed by extended treatment period (Week 16 to Week 52), followed by post treatment period for a maximum of 24 weeks.
Washout period occurred for only Adalimumab group for 6 weeks (Week 14 to Week 20).

Pre-assignment

Screening details:

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

Period 1

Period 1 title	Blinded Treatment 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 by subcutaneous injection.

Arm type	Experimental
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 by subcutaneous injection.

Arm title	Adalimumab

Arm description:

Blinded Treatment Period:Participants received 40mg Adalimumab every two weeks by SC injection.

Arm type	Active comparator
Investigational medicinal product name	Adalimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received 40mg Adalimumab by subcutaneous injection every two weeks.

Arm title	IXE80Q2W

Arm description:

Participants received starting dose of either 80 milligrams (mg) or 160mg Ixekizumab at week 0 followed by 80mg Ixekizumab every two weeks by subcutaneous injection.

Arm type	Experimental

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

Dosage and administration details:

Participants received starting dose of either 80 milligrams (mg) or 160mg Ixekizumab at week 0 followed by 80mg Ixekizumab every two weeks by subcutaneous injection.

Arm title	IXE80Q4W

Arm description:

Participants received starting dose of either 80 milligrams (mg) or 160mg Ixekizumab at week 0 followed by 80mg Ixekizumab every four weeks by subcutaneous injection.

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

Dosage and administration details:

Participants received starting dose of either 80 milligrams (mg) or 160mg Ixekizumab at week 0 followed by 80mg Ixekizumab every four weeks by subcutaneous injection.

Number of subjects in period 1	Placebo (PBO)	Adalimumab	IXE80Q2W
Started	86	90	83
Received at least one dose of study drug	86	90	83
Completed	86	88	79
Not completed	0	2	4
Consent withdrawn by subject	-	1	1
Adverse event, non-fatal	-	1	3
Lack of efficacy	-	-	-

Number of subjects in period 1	IXE80Q4W
Started	81
Received at least one dose of study drug	81
Completed	78
Not completed	3
Consent withdrawn by subject	2
Adverse event, non-fatal	-
Lack of efficacy	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 received starting dose of 160mg Ixekizumab at week 16 followed by 80mg Ixekizumab either every two weeks (Q2W) or every four weeks (Q4W) by subcutaneous (SC) injection.

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

Dosage and administration details:

Participants received starting dose of 160mg Ixekizumab at week 16 followed by 80mg Ixekizumab either every two weeks (Q2W) or every four weeks (Q4W) by subcutaneous (SC) injection during extended treatment period.

Arm title	Adalimumab/PBO/IXE

Arm description:

Participants who received Adalimumab in blinded treatment period received 80mg Ixekizumab either Q2W or Q4W by SC injection during extension treatment period.
Washout Period: Participants received placebo for 6 weeks.

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

Dosage and administration details:

Participants received 80mg Ixekizumab either Q2W or Q4W by SC injection.

Arm title	IXE80Q2W/IXE80Q2W

Arm description:

Participants received starting dose of either 80 milligrams (mg) or 160mg Ixekizumab at week 0 followed by 80mg Ixekizumab every two weeks by subcutaneous injection.

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

Dosage and administration details:

Participants received starting dose of either 80 milligrams (mg) or 160mg Ixekizumab at week 0 followed by 80mg Ixekizumab every two weeks by subcutaneous injection.

Arm title	IXE80Q4W/IXE80Q4W

Arm description:

Participants received starting dose of either 80 milligrams (mg) or 160mg Ixekizumab at week 0 followed by 80mg Ixekizumab every four weeks by subcutaneous injection.

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

Dosage and administration details:

Participants received starting dose of either 80 milligrams (mg) or 160mg Ixekizumab at week 0 followed by 80mg Ixekizumab every two weeks by subcutaneous injection.

Number of subjects in period 2[1]	PBO/IXE	Adalimumab/PBO/IXE	IXE80Q2W/IXE80Q2W
Started	86	86	79
Completed	83	80	74
Not completed	3	6	5
Consent withdrawn by subject	1	2	3
Adverse event, non-fatal	2	3	2
Lack of efficacy	-	1	-

Number of subjects in period 2[1]	IXE80Q4W/IXE80Q4W
Started	78
Completed	72
Not completed	6
Consent withdrawn by subject	5
Adverse event, non-fatal	1
Lack of efficacy	-

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: Adalimumab group has two participants in the washout period discontinuing the study. 1 participant with Lack if efficacy, 1 participant with consent with drawn by subject.

Period 3

Period 3 title	Follow-up Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes

Arm title	Placebo (PBO)
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	
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	

Number of subjects in period 3[2]	Placebo (PBO)	IXE80Q2W	IXE80Q4W
Started	1	24	16
Completed	0	11	8
Not completed	1	13	8
Consent withdrawn by subject	1	5	4
Adverse event, non-fatal	-	8	2
Lost to follow-up	-	-	1
Lack of efficacy	-	-	1

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 completed study were eligible to enroll RHBY directly without entering Follow-Up period.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo (PBO)
Reporting group description:	
Participants received placebo every two weeks by subcutaneous injection.	

Reporting group title	Adalimumab
Reporting group description:	
Blinded Treatment Period:Participants received 40mg Adalimumab every two weeks by SC injection.	

Reporting group title	IXE80Q2W
Reporting group description:	
Participants received starting dose of either 80 milligrams (mg) or 160mg Ixekizumab at week 0 followed by 80mg Ixekizumab every two weeks by subcutaneous injection.	
Reporting group title	IXE80Q4W
Reporting group description:	
Participants received starting dose of either 80 milligrams (mg) or 160mg Ixekizumab at week 0 followed by 80mg Ixekizumab every four weeks by subcutaneous injection.	

Reporting group values	Placebo (PBO)	Adalimumab	IXE80Q2W
Number of subjects	86	90	83
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	42.7	41.8	41.3
standard deviation	± 12.01	± 11.44	± 11.17
Gender categorical Units: Subjects			
Female	15	17	19
Male	71	73	64
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	11	7	8
Not Hispanic or Latino	67	74	68
Unknown or Not Reported	8	9	7
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	4	2	4

Asian	28	29	25
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	52	57	52
More than one race	2	2	2
Unknown or Not Reported	0	0	0
Region of Enrollment Units: Subjects			
South Korea	10	14	12
Netherlands	0	2	2
United States	5	3	4
Japan	3	3	0
Taiwan	13	12	13
Germany	0	2	1
Canada	2	3	2
Hungary	3	2	2
Mexico	8	7	8
Poland	16	15	15
Russia	12	13	11
Czech Republic	14	14	13

Reporting group values	IXE80Q4W	Total	
Number of subjects	81	340	
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	41.0		
standard deviation	± 12.13	-	
Gender categorical Units: Subjects			
Female	13	64	
Male	68	276	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	8	34	
Not Hispanic or Latino	66	275	
Unknown or Not Reported	7	31	
Race (NIH/OMB) Units: Subjects			

American Indian or Alaska Native	4	14	
Asian	25	107	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	52	213	
More than one race	0	6	
Unknown or Not Reported	0	0	
Region of Enrollment Units: Subjects			
South Korea	11	47	
Netherlands	0	4	
United States	3	15	
Japan	1	7	
Taiwan	13	51	
Germany	0	3	
Canada	2	9	
Hungary	3	10	
Mexico	7	30	
Poland	16	62	
Russia	12	48	
Czech Republic	13	54	

End points

End points reporting groups

Reporting group title	Placebo (PBO)

Reporting group description:

Participants received placebo every two weeks by subcutaneous injection.

Reporting group title	Adalimumab

Reporting group description:

Blinded Treatment Period:Participants received 40mg Adalimumab every two weeks by SC injection.

Reporting group title	IXE80Q2W

Reporting group description:

Participants received starting dose of either 80 milligrams (mg) or 160mg Ixekizumab at week 0 followed by 80mg Ixekizumab every two weeks by subcutaneous injection.

Reporting group title	IXE80Q4W

Reporting group description:

Participants received starting dose of either 80 milligrams (mg) or 160mg Ixekizumab at week 0 followed by 80mg Ixekizumab every four weeks by subcutaneous injection.

Reporting group title	PBO/IXE

Reporting group description:

Participants received starting dose of 160mg Ixekizumab at week 16 followed by 80mg Ixekizumab either every two weeks (Q2W) or every four weeks (Q4W) by subcutaneous (SC) injection.

Reporting group title	Adalimumab/PBO/IXE

Reporting group description:

Participants who received Adalimumab in blinded treatment period received 80mg Ixekizumab either Q2W or Q4W by SC injection during extension treatment period.
Washout Period: Participants received placebo for 6 weeks.

Reporting group title	IXE80Q2W/IXE80Q2W

Reporting group description:

Participants received starting dose of either 80 milligrams (mg) or 160mg Ixekizumab at week 0 followed by 80mg Ixekizumab every two weeks by subcutaneous injection.

Reporting group title	IXE80Q4W/IXE80Q4W

Reporting group description:

Participants received starting dose of either 80 milligrams (mg) or 160mg Ixekizumab at week 0 followed by 80mg Ixekizumab every four weeks by subcutaneous injection.

Reporting group title	Placebo (PBO)

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.

Reporting group title	IXE80Q4W

Reporting group description:

Participants did not receive any intervention during Follow-up period.

Subject analysis set title	PBO/IXE
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received placebo every two weeks during blinded treatment period and starting dose of 160mg Ixekizumab at week 16 followed by 80mg Ixekizumab either Q2W or Q4W extended treatment period by subcutaneous injection.

Subject analysis set title	Adalimumab/IXE
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received 40mg Adalimumab every two weeks during blinded treatment period and 80mg Ixekizumab either Q2W or Q4W during extended treatment period by subcutaneous injection.

Subject analysis set title	IXE80Q4W/IXE80Q4W
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received starting dose of either 80 milligrams (mg) or 160mg Ixekizumab at week 0 followed by 80mg Ixekizumab every four weeks during blinded treatment and extension period by subcutaneous injection.

Subject analysis set title	IXE80Q2W/IXE80Q2W
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received starting dose of either 80 milligrams (mg) or 160mg Ixekizumab at week 0 followed by 80mg Ixekizumab every two weeks during blinded treatment and extension period by subcutaneous injection.

Subject analysis set title	IXE160/80Q4W
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received starting dose of 160mg Ixekizumab at week 0 followed by 80mg Ixekizumab every four weeks by subcutaneous injection.

Subject analysis set title	IXE160/80Q2W
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received starting dose of 160mg Ixekizumab at week 0 followed by 80mg 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 greater than or equal to (>=) 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 domains.
1.Patient Global: How active was your spondylitis on average during the last week? score range 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: Participant is asked to rate the difficulty associated with 10 individual basic functional activities. Participants response is captured using NRS scale (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	Primary

End point timeframe:

Week 16

End point values	Placebo (PBO)	Adalimumab	IXE80Q2W	IXE80Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86[1]	90	83	81
Units: percentage of participants				
number (not applicable)	18.4	35.6	51.8	48.1

Notes:

[1] - Total participants 87, one participant who did not receive study drug is included in the analysis.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (PBO) v Adalimumab
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.005
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.35
upper limit	5.52

Notes:

[2] - Total participants 177. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo (PBO) v IXE80Q4W
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.2
upper limit	9.03

Notes:

[3] - Total participants 168. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo (PBO) v IXE80Q2W

Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.52
upper limit	10.28

Notes:

[4] - Total participants 170. one participant who did not receive study drug is included in the analysis.

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 in ≥3 of 4 following 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 range 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: Participant is asked to rate the difficulty associated with 10 individual basic functional activities. Participants response is captured using NRS scale (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).

Analysis Population Description (APD): All Randomized Participants.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo (PBO)	Adalimumab	IXE80Q2W	IXE80Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86	90	83	81
Units: percentage of participants				
number (not applicable)	40.2	58.9	68.7	64.2

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Adalimumab v Placebo (PBO)

Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.007
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.25
upper limit	4.23

Notes:

[5] - Total participants 177. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo (PBO) v IXE80Q4W
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	= 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.48
upper limit	5.24

Notes:

[6] - Total participants 168. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo (PBO) v IXE80Q2W
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.79
upper limit	6.41

Notes:

[7] - Total participants 170. one participant who did not receive study drug is included in the analysis.

Secondary: Change from Baseline in Ankylosing Spondylitis Disease Activity Score

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

End point description:

ASDAS is a composite index to assess disease activity in AS. The parameters used for the ASDAS (with CRP as acute phase reactant) are the following:

1.Total back pain
2.Patient global
3.Peripheral pain/swelling
4.Duration of morning stiffness
5.CRP in mg/L The ASDAScrp is calculated with the following equation: 0.121 × total back pain + 0.110 × patient global + 0.073 × peripheral pain/swelling + 0.058 × duration of morning stiffness + 0.579 × Ln(CRP+1). CRP is in mg/liter, the range of other variables is from 0 to 10.Data from five variables combined to yield a score (0.6361 to no defined upper limit), where higher scores indicated higher disease activity. Ln represents the natural logarithm.

Least Square (LS) Mean was calculated using mixed model repeated measures (MMRM) model with treatment, geographic region, baseline CRP status, 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 (PBO)	Adalimumab	IXE80Q2W	IXE80Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86[8]	90	83	81
Units: score on a scale				
least squares mean (standard error)	-0.46 (± 0.099)	-1.30 (± 0.096)	-1.37 (± 0.101)	-1.43 (± 0.102)

Notes:

[8] - Total participants 87, one participant who did not receive study drug is included in the analysis.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (PBO) v Adalimumab
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.11
upper limit	-0.57
Variability estimate	Standard error of the mean
Dispersion value	0.137

Notes:

[9] - Total participants 177. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo (PBO) v IXE80Q4W
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	superiority[10]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.25
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.141

Notes:

[10] - Total participants 168. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo (PBO) v IXE80Q2W
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority[11]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.18
upper limit	-0.63
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[11] - Total participants 170. one participant who did not receive study drug is included in the analysis.

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 measuring discomfort, pain, and fatigue. 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).
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 (PBO)	Adalimumab	IXE80Q2W	IXE80Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86[12]	90	83	81
Units: percentage of participants				
number (not applicable)	17.2	32.2	43.4	42.0

Notes:
[12] - Total participants 87, one participant who did not receive study drug is included in the analysis.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (PBO) v Adalimumab
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	= 0.012
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.23
upper limit	5.21

Notes:
[13] - Total participants 177. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo (PBO) v IXE80Q4W
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	superiority[14]
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.82
upper limit	7.7

Notes:

[14] - Total participants 168. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo (PBO) v IXE80Q2W
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority[15]
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.91
upper limit	7.98

Notes:

[15] - Total participants 170. one participant who did not receive study drug is included in the analysis.

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 participants functional baseline and subsequent response to treatment. To complete the BASFI, a participant is asked to rate the difficulty associated with 10 individual basic functional activities. Participants respond to each question using an NRS scale (range 0 to 10) with a higher score indicating worse function. The participants final BASFI score is the mean of the 10 item scores has a possible minimum value of 0 and a possible maximum value of 10, with a higher score indicating worse function.

LSMean was calculated using MMRM model with treatment, geographic region, baseline CRP status, 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 (PBO)	Adalimumab	IXE80Q2W	IXE80Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86[16]	90	83	81
Units: score on a scale				
least squares mean (standard error)	-1.16 (± 0.215)	-2.14 (± 0.209)	-2.43 (± 0.219)	-2.39 (± 0.222)

Notes:

[16] - Total participants 87, one participant who did not receive study drug is included in the analysis.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (PBO) v Adalimumab
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority[17]
P-value	= 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.56
upper limit	-0.39
Variability estimate	Standard error of the mean
Dispersion value	0.299

Notes:

[17] - Total participants 177. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 2
Comparison groups	IXE80Q4W v Placebo (PBO)
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	superiority[18]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.83
upper limit	-0.62
Variability estimate	Standard error of the mean
Dispersion value	0.307

Notes:

[18] - Total participants 168. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo (PBO) v IXE80Q2W
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority[19]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-1.27

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.86
upper limit	-0.67
Variability estimate	Standard error of the mean
Dispersion value	0.304

Notes:

[19] - Total participants 170. one participant who did not receive study drug is included in the analysis.

Secondary: Percentage of Participants Achieving ASDAS Inactive Disease

End point title	Percentage of Participants Achieving ASDAS Inactive Disease

End point description:

ASDAS is a composite index to assess disease activity in AS. The parameters used for the ASDAS (with CRP as acute phase reactant) are the following:
1.Total back pain
2.Patient global
3.Peripheral pain/swelling
4.Duration of morning stiffness
5.CRP in mg/L The ASDAScrp is calculated with the following equation: 0.121 × total back pain + 0.110 × patient global + 0.073 × peripheral pain/swelling + 0.058 × duration of morning stiffness + 0.579 × Ln(CRP+1). CRP is in mg/liter, the range of other variables is from 0 to 10.Data from five variables combined to yield a score (0.6361 to no defined upper limit), where higher scores indicated higher disease activity. Ln represents the natural logarithm. 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 (PBO)	Adalimumab	IXE80Q2W	IXE80Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86[20]	90	83	81
Units: percentage of Participants				
number (not applicable)	2.3	15.6	10.8	16.0

Notes:

[20] - Total participants 87, one participant who did not receive study drug is included in the analysis.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Adalimumab v Placebo (PBO)
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority[21]
P-value	= 0.009
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	7.62

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.67
upper limit	34.68

Notes:

[21] - Total participants 177. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo (PBO) v IXE80Q4W
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	superiority[22]
P-value	= 0.007
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	8.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.75
upper limit	36.83

Notes:

[22] - Total participants 168. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo (PBO) v IXE80Q2W
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority[23]
P-value	= 0.041
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	24.49

Notes:

[23] - Total participants 170. one participant who did not receive study drug is included in the analysis.

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 Berlin modification of Ankylosing Spondylitis spine MRI score for activity (ASspiMRI) scoring technique assesses inflammation in each of 23 disco-vertebral units (DVU). All 23 disco-vertebral units

(DVU) of the spine (from C2 to S1) are scored for 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.

LSMean was calculated using ANCOVA model with treatment, geographic region, baseline CRP status and baseline value as fixed factors.

APD: All Randomized Participants with baseline and week 16 Berlin score.

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

End point values	Placebo (PBO)	Adalimumab	IXE80Q2W	IXE80Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	81	82	76	78
Units: score on a scale				
least squares mean (standard error)	-0.15 (± 0.323)	-2.92 (± 0.314)	-2.54 (± 0.330)	-2.77 (± 0.328)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (PBO) v Adalimumab
Number of subjects included in analysis	163
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LSMean Difference
Point estimate	-2.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.7
upper limit	-1.9
Variability estimate	Standard error of the mean
Dispersion value	0.447

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo (PBO) v IXE80Q4W

Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LSMean Difference
Point estimate	-2.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	-1.7
Variability estimate	Standard error of the mean
Dispersion value	0.45

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo (PBO) v IXE80Q2W
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LSMean Difference
Point estimate	-2.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	-1.5
Variability estimate	Standard error of the mean
Dispersion value	0.452

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 calculated using MMRM model with treatment, geographic region, baseline CRP status, 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 (PBO)	Adalimumab	IXE80Q2W	IXE80Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86[24]	90	83	81
Units: score on a scale				
least squares mean (standard error)				
PCS	3.6432 (± 0.7530)	6.9005 (± 0.7310)	7.9686 (± 0.7665)	7.6952 (± 0.7768)
MCS	2.1229 (± 0.8431)	2.5550 (± 0.8225)	2.5696 (± 0.8650)	2.7502 (± 0.8763)

Notes:
[24] - Total participants 87, one participant who did not receive study drug is included in the analysis.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: PCS	
Comparison groups	Placebo (PBO) v Adalimumab
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority[25]
P-value	= 0.002
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	3.2574
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2041
upper limit	5.3106
Variability estimate	Standard error of the mean
Dispersion value	1.0437

Notes:
[25] - Total participants 177. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: PCS	
Comparison groups	Placebo (PBO) v IXE80Q4W

Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	superiority[26]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	4.052
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.9432
upper limit	6.1608
Variability estimate	Standard error of the mean
Dispersion value	1.072

Notes:

[26] - Total participants 168. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
PCS	
Comparison groups	Placebo (PBO) v IXE80Q2W
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority[27]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	4.3254
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.2321
upper limit	6.4186
Variability estimate	Standard error of the mean
Dispersion value	1.0641

Notes:

[27] - Total participants 170. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 4
Statistical analysis description:	
MCS	
Comparison groups	Placebo (PBO) v Adalimumab
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority[28]
P-value	= 0.713
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	0.4321

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8732
upper limit	2.7373
Variability estimate	Standard error of the mean
Dispersion value	1.1718

Notes:

[28] - Total participants 177. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 5
Statistical analysis description:	
MCS	
Comparison groups	Placebo (PBO) v IXE80Q4W
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	superiority[29]
P-value	= 0.602
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	0.6273
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7387
upper limit	2.9934
Variability estimate	Standard error of the mean
Dispersion value	1.2028

Notes:

[29] - Total participants 167. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 6
Statistical analysis description:	
MCS	
Comparison groups	Placebo (PBO) v IXE80Q2W
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority[30]
P-value	= 0.709
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	0.4467
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9097
upper limit	2.803
Variability estimate	Standard error of the mean
Dispersion value	1.1978

Notes:

[30] - Total participants 169. one participant who did not receive study drug is included in the analysis.

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

End point title	Change from Baseline in ASAS Health Index (ASAS HI)

End point description:

ASAS HI is a disease-specific health-index instrument designed to assess the impact of interventions for SpA, including axSpA. The 17-item instrument has scores ranging from 0 (good health) to 17 (poor health). Each item consists of one question that the participant needs to respond to with either "I agree" (score of 1) or "I do not agree" (score of 0). A score of "1" is given where the item is affirmed, indicating adverse health. All item scores are summed to give a total score or index.

LSMean was calculated using MMRM model with treatment, geographic region, baseline CRP status, 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 (PBO)	Adalimumab	IXE80Q2W	IXE80Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86[31]	90	83	81
Units: score on a scale				
least squares mean (standard error)	-1.25 (± 0.300)	-2.30 (± 0.292)	-2.74 (± 0.306)	-2.36 (± 0.311)

Notes:

[31] - Total participants 87, one participant who did not receive study drug is included in the analysis.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (PBO) v Adalimumab
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority[32]
P-value	= 0.012
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.87
upper limit	-0.23
Variability estimate	Standard error of the mean
Dispersion value	0.416

Notes:

[32] - Total participants 177. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo (PBO) v IXE80Q4W
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	superiority[33]
P-value	= 0.01
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.95
upper limit	-0.27
Variability estimate	Standard error of the mean
Dispersion value	0.428

Notes:

[33] - Total participants 168. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 3
Comparison groups	IXE80Q2W v Placebo (PBO)
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority[34]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-1.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.32
upper limit	-0.66
Variability estimate	Standard error of the mean
Dispersion value	0.423

Notes:

[34] - Total participants 170. one participant who did not receive study drug is included in the analysis.

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

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

End point description:

High sensitivity CRP is the measure of acute phase reactant. It will be measured with a high sensitivity assay at the central laboratory to help assess the effect of Ixekizumab on disease activity.

LSMean was calculated using MMRM model with treatment, geographic region, baseline CRP status, 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 (PBO)	Adalimumab	IXE80Q2W	IXE80Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86[35]	90	83	81
Units: Milliragm per Litre (mg/mL)				
least squares mean (standard error)	1.426 (± 1.9244)	-7.202 (± 1.8688)	-6.565 (± 1.9582)	-5.209 (± 1.9803)

Notes:
[35] - Total participants 87, one participant who did not receive study drug is included in the analysis.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (PBO) v Adalimumab
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority[36]
P-value	= 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-8.628
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.885
upper limit	-3.371
Variability estimate	Standard error of the mean
Dispersion value	2.6724

Notes:
[36] - Total participants 177. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo (PBO) v IXE80Q4W
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	superiority[37]
P-value	= 0.016
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-6.635
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.033
upper limit	-1.238

Variability estimate	Standard error of the mean
Dispersion value	2.7438

Notes:

[37] - Total participants 168. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo (PBO) v IXE80Q2W
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority[38]
P-value	= 0.004
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-7.991
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.351
upper limit	-2.631
Variability estimate	Standard error of the mean
Dispersion value	2.7248

Notes:

[38] - Total participants 169. one participant who did not receive study drug is included in the analysis.

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

End point title	Change from Baseline in Mobility on the Bath Ankylosing Spondylitis Metrology Index (BASMI)

End point description:

The BASMI is a combined index comprising the following 5 clinical measurements of spinal mobility in participants with rad-axSpA.
1) Lateral spinal flexion
2)Tragus-to-wall distance
3) Lumbar flexion (modified Schrober)
4) Maximal intermalleolar distance
5)Cervical rotation.
The BASMI includes these 5 measurements that are each scaled to a score of 0 to 10 depending on the result of the assessment (BASMI linear function). The average score of the 5 assessments gives the BASMI linear result. The higher the BASMI score the more severe the participants limitation of movement due to their AS.
LSMean was calculated using MMRM model with treatment, geographic region, baseline CRP status, 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 (PBO)	Adalimumab	IXE80Q2W	IXE80Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86[39]	90	83	81
Units: score on a scale				
least squares mean (standard error)	-0.080 (± 0.0826)	-0.447 (± 0.0800)	-0.408 (± 0.0840)	-0.447 (± 0.0858)

Notes:

[39] - Total participants 87, one participant who did not receive study drug is included in the analysis.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (PBO) v Adalimumab
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority[40]
P-value	= 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.367
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.592
upper limit	-0.142
Variability estimate	Standard error of the mean
Dispersion value	0.1143

Notes:

[40] - Total participants 177. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo (PBO) v IXE80Q4W
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	superiority[41]
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.422
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.655
upper limit	-0.189
Variability estimate	Standard error of the mean
Dispersion value	0.1184

Notes:

[41] - Total participants 168. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 3

Comparison groups	Placebo (PBO) v IXE80Q2W
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority[42]
P-value	= 0.005
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.329
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.558
upper limit	-0.099
Variability estimate	Standard error of the mean
Dispersion value	0.1167

Notes:

[42] - Total participants 170. one participant who did not receive study drug is included in the analysis.

Secondary: Change from Baseline in Chest Expansion

End point title	Change from Baseline in Chest Expansion

End point description:

While participants have their hands resting on or behind the head, the assessor has measured the chest's encircled length by centimeter at the fourth intercostal level anteriorly. The difference between maximal inspiration and expiration in centimeters was recorded. Two tries were recorded. The better measurement (larger difference) of 2 tries (in centimeters) was used for analyses.

LSMean was calculated using MMRM model with treatment, geographic region, baseline CRP status, 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 (PBO)	Adalimumab	IXE80Q2W	IXE80Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86[43]	90	83	81
Units: Centimeters (cm)				
least squares mean (standard error)	0.06 (± 0.152)	0.70 (± 0.148)	0.67 (± 0.155)	0.49 (± 0.158)

Notes:

[43] - Total participants 87, one participant who did not receive study drug is included in the analysis.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (PBO) v Adalimumab

Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority[44]
P-value	= 0.003
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.22
upper limit	1.05
Variability estimate	Standard error of the mean
Dispersion value	0.211

Notes:

[44] - Total participants 177. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo (PBO) v IXE80Q4W
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	superiority[45]
P-value	= 0.051
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.86
Variability estimate	Standard error of the mean
Dispersion value	0.219

Notes:

[45] - Total participants 168. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo (PBO) v IXE80Q2W
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority[46]
P-value	= 0.005
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.18
upper limit	1.03

Variability estimate	Standard error of the mean
Dispersion value	0.215

Notes:

[46] - Total participants 170. one participant who did not receive study drug is included in the analysis.

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.

LSMean was calculated using MMRM model with treatment, geographic region, baseline CRP status, 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 (PBO)	Adalimumab	IXE80Q2W	IXE80Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86[47]	90	83	81
Units: cm				
least squares mean (standard error)	-0.06 (± 0.232)	-0.72 (± 0.225)	-0.73 (± 0.236)	-0.69 (± 0.240)

Notes:

[47] - Total participants 87, one participant who did not receive study drug is included in the analysis.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (PBO) v Adalimumab
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority[48]
P-value	= 0.039
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.03
Variability estimate	Standard error of the mean
Dispersion value	0.321

Notes:

[48] - Total participants 177. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo (PBO) v IXE80Q4W
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	superiority[49]
P-value	= 0.057
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.28
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.33

Notes:

[49] - Total participants 168. one participant who did not receive study drug is included in the analysis.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo (PBO) v IXE80Q2W
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority[50]
P-value	= 0.042
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.31
upper limit	-0.03
Variability estimate	Standard error of the mean
Dispersion value	0.327

Notes:

[50] - Total participants 170. one participant who did not receive study drug is included in the analysis.

Secondary: Change from Baseline in MRI sacroiliac joint(s) (SIJ) Spondyloarthritis Research Consortium of Canada (SPARCC) Score

End point title	Change from Baseline in MRI sacroiliac joint(s) (SIJ) Spondyloarthritis Research Consortium of Canada (SPARCC) Score

End point description:

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

APD: All randomized participants with baseline and week 16 SPARCC score.

End point type	Secondary

End point timeframe:
Baseline, Week 16

End point values	Placebo (PBO)	Adalimumab	IXE80Q2W	IXE80Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	81	82	77	78
Units: score on a scale				
least squares mean (standard error)	0.92 (± 0.582)	-4.21 (± 0.568)	-4.25 (± 0.591)	-3.97 (± 0.590)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (PBO) v Adalimumab
Number of subjects included in analysis	163
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LSMean Difference
Point estimate	-5.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.7
upper limit	-3.5
Variability estimate	Standard error of the mean
Dispersion value	0.806

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo (PBO) v IXE80Q4W
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LSMean Difference
Point estimate	-4.89

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.5
upper limit	-3.3
Variability estimate	Standard error of the mean
Dispersion value	0.812

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo (PBO) v IXE80Q2W
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LSMean Difference
Point estimate	-5.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.8
upper limit	-3.6
Variability estimate	Standard error of the mean
Dispersion value	0.816

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.

LSMean was calculated using MMRM model with treatment, geographic region, baseline CRP status, 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 (PBO)	Adalimumab	IXE80Q2W	IXE80Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	51	50	49
Units: score on a scale				
least squares mean (standard error)	-2.1 (± 0.34)	-2.6 (± 0.34)	-2.4 (± 0.35)	-2.3 (± 0.36)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (PBO) v Adalimumab
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.317
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.48

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo (PBO) v IXE80Q4W
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.683
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.48

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo (PBO) v IXE80Q2W

Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.48

Secondary: Change from Baseline in SPARCC Enthesitis Score

End point title	Change from Baseline in SPARCC Enthesitis Score

End point description:

The SPARCC enthesitis is an index used to measure the severity of enthesitis. The SPARCC assesses 16 sites for enthesitis using a score of "0" for no activity or "1" for activity. Sites assessed include Medial epicondyle (left/right [L/R]), Lateral epicondyle (L/R), Supraspinatus insertion into greater tuberosity of humerus (L/R), Greater trochanter (L/R), Quadriceps insertion into superior border of patella (L/R), Patellar ligament insertion into inferior pole of patella or tibial tubercle (L/R), Achilles tendon insertion into calcaneum (L/R),
and Plantar fascia insertion into calcaneum (L/R). The SPARCC is the sum of all site scores (range 0 to 16). Higher scores indicate more severe enthesitis.
LSMean was calculated using MMRM model with treatment, geographic region, baseline CRP status, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors.

APD: All Randomized Participants with baseline SPARCC score > 0.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo (PBO)	Adalimumab	IXE80Q2W	IXE80Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	40	35	40
Units: score on a scale				
least squares mean (standard error)	-2.1 (± 0.40)	-2.9 (± 0.40)	-2.6 (± 0.43)	-2.7 (± 0.40)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (PBO) v Adalimumab

Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.154
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.56

Statistical analysis title	Statistical Analysis 2
Comparison groups	IXE80Q4W v Placebo (PBO)
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.255
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.56

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo (PBO) v IXE80Q2W
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.398
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	0.7

Variability estimate	Standard error of the mean
Dispersion value	0.58

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

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

End point description:

The number of tender and painful joints was determined by examination of 46 joints (23 joints on each side of the participants body. The 46 joints are assessed and classified as tender or not tender. sum of all joints checked to be tender/painful divided by number of evaluable joints which is multiplied by 46 to obtain TJC score. The scores ranges from 0 (no tender/painful joints) to 46 (all joints tender/painful).

LSMean was calculated using MMRM model with treatment, geographic region, baseline CRP status, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors.

APD: All Randomized Participants with baseline TJC > 0.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo (PBO)	Adalimumab	IXE80Q2W	IXE80Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	49	45	44
Units: score on a scale				
least squares mean (standard error)	-2.0 (± 0.53)	-2.2 (± 0.55)	-3.3 (± 0.58)	-2.5 (± 0.58)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (PBO) v Adalimumab
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.783
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	1.3
Variability estimate	Standard error of the mean
Dispersion value	0.76

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo (PBO) v IXE80Q4W
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.55
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.78

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo (PBO) v IXE80Q2W
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.091
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	0.2
Variability estimate	Standard error of the mean
Dispersion value	0.77

Secondary: Number of Participants with Anterior Uveitis or Uveitis Flares

End point title	Number of Participants with Anterior Uveitis or Uveitis Flares

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:
Baseline through Week 16

End point values	Placebo (PBO)	Adalimumab	IXE80Q2W	IXE80Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86[51]	90	83	81
Units: Count of Participants				
number (not applicable)	0	0	0	1

Notes:

[51] - Total participants 87, one participant who did not receive study drug is included in the analysis.

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The Fatigue Severity NRS is a participant-administered, single-item, 11-point horizontal scale anchored at 0 and 10, with 0 representing "no fatigue" and 10 representing "as bad as you can imagine". Participants rate their fatigue (feeling tired or worn out) by circling the one number that describes their worst level of fatigue during the previous 24 hours.
LSMean was calculated using MMRM model with treatment, geographic region, baseline CRP status, 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 (PBO)	Adalimumab	IXE80Q2W	IXE80Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86[52]	90	83	81
Units: score on a scale				
least squares mean (standard error)	-1.4 (± 0.23)	-2.2 (± 0.23)	-2.1 (± 0.24)	-2.5 (± 0.24)

Notes:

[52] - Total participants 87, one participant who did not receive study drug is included in the analysis.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (PBO) v Adalimumab

Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.027
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.32

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo (PBO) v IXE80Q4W
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	-0.4
Variability estimate	Standard error of the mean
Dispersion value	0.33

Statistical analysis title	Statistical Analysis 3
Comparison groups	IXE80Q2W v Placebo (PBO)
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.035
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0

Variability estimate	Standard error of the mean
Dispersion value	0.33

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 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. Participants report the number 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.
LSMean was calculated using MMRM model with treatment, geographic region, baseline CRP status, 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 (PBO)	Adalimumab	IXE80Q2W	IXE80Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86[53]	90	83	81
Units: score on a scale				
least squares mean (standard error)	-1.5 (± 0.41)	-2.7 (± 0.40)	-3.0 (± 0.42)	-2.5 (± 0.43)

Notes:

[53] - Total participants 87, one participant who did not receive study drug is included in the analysis.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (PBO) v Adalimumab
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.041
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.57

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo (PBO) v IXE80Q4W
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.125
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.59

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo (PBO) v IXE80Q2W
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.013
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	-0.3
Variability estimate	Standard error of the mean
Dispersion value	0.58

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. Greater scores indicate greater impairment and less productivity.
LSMean was calculated using ANCOVA model with treatment, geographic region, baseline CRP status and baseline value as fixed factors.
APD: All Randomized Participants with baseline and week 16 WPAI score.

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

End point values	Placebo (PBO)	Adalimumab	IXE80Q2W	IXE80Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86	88	83	80
Units: score on a scale				
least squares mean (standard error)				
Overall Work Impairment Score	-17.82 (± 3.254)	-21.44 (± 2.921)	-24.06 (± 3.299)	-21.36 (± 3.061)
Percentage of Activity Impairment	-14.1 (± 2.28)	-21.1 (± 2.22)	-23.4 (± 2.30)	-23.0 (± 2.35)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Overall Work Impairment Score Subjects in analysis: 110	
Comparison groups	Placebo (PBO) v Adalimumab
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.408
Method	ANCOVA
Parameter estimate	LSMean Difference
Point estimate	-3.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.21
upper limit	4.98
Variability estimate	Standard error of the mean
Dispersion value	4.36

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Overall Work Impairment Score. Subjects in Analysis: 105	
Comparison groups	Placebo (PBO) v IXE80Q4W

Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.422
Method	ANCOVA
Parameter estimate	LSMean Difference
Point estimate	-3.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.2
upper limit	5.13
Variability estimate	Standard error of the mean
Dispersion value	4.393

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: Overall Work Impairment Score Subjects in this Analysis: 97	
Comparison groups	Placebo (PBO) v IXE80Q2W
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.175
Method	ANCOVA
Parameter estimate	LSMean Difference
Point estimate	-6.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.27
upper limit	2.8
Variability estimate	Standard error of the mean
Dispersion value	4.582

Statistical analysis title	Statistical Analysis 4
Statistical analysis description: Percentage of Activity Impairment	
Comparison groups	Placebo (PBO) v Adalimumab
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LSMean Difference
Point estimate	-7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.2
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	3.16

Statistical analysis title	Statistical Analysis 5
Statistical analysis description: Percentage of Activity Impairment	
Comparison groups	Placebo (PBO) v IXE80Q4W
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LSMean Difference
Point estimate	-8.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.2
upper limit	-2.5
Variability estimate	Standard error of the mean
Dispersion value	3.22

Statistical analysis title	Statistical Analysis 6
Statistical analysis description: Percentage of Activity Impairment	
Comparison groups	Placebo (PBO) v IXE80Q2W
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LSMean Difference
Point estimate	-9.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.5
upper limit	-3
Variability estimate	Standard error of the mean
Dispersion value	3.19

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).. ASAS-NSAID score=(equivalent NSAID score)x(days of intake during PI)x(days per week)/(PI in days). Higher scores indicate greater NSAIDs intake. 0= no intake, 100 = equivalent NSAID intake.

Participants in Extended Treatment Period Population Who had NSAID Intake at Baseline.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	PBO/IXE	Adalimumab/IXE	IXE80Q4W/IXE80Q4W	IXE80Q2W/IXE80Q2W
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	78	80	71	76
Units: score on a scale				
arithmetic mean (standard deviation)	-10.28 (± 27.472)	-5.91 (± 20.861)	-7.62 (± 25.430)	-9.91 (± 27.940)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Anti Ixekizumab Antibodies

End point title	Number of Participants with Anti Ixekizumab Antibodies

End point description:

A treatment emergent - antidrug antibody (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.

APD: All randomized participants.

End point type	Secondary

End point timeframe:

Week 16

End point values	Placebo (PBO)	Adalimumab	IXE80Q2W	IXE80Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86	90	83	81
Units: participants				
number (not applicable)	2	5	2	2

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

APD: All randomized participants who received at least one dose of Ixekizumab.

End point type	Secondary

End point timeframe:

Week 16

End point values	IXE160/80Q4W	IXE160/80Q2W		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	39	38		
Units: microgram per millilitre (µg/mL)				
geometric mean (geometric coefficient of variation)	3.88 (± 55)	11.3 (± 43)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The number of swollen joints was determined by examination of 44 joints (22 joints on each side of the participants body. The 44 joints are assessed and classified as swollen or not swollen. "sum of all joints checked to be swollen" divided by "number of evaluable joints" and then multiplied by 44 to obtain SJC score. The SJC score ranges from 0 (no swollen joints) to 44 (all joints swollen).

LSMean was calculated using MMRM model with treatment, geographic region, baseline CRP status, baseline value, visit, baseline value-by-visit, and treatment-by-visit interaction as fixed factors.

APD: All Randomized Participants with baseline SJC > 0.

End point type	Secondary

End point timeframe:
Baseline, Week 16

End point values	Placebo (PBO)	Adalimumab	IXE80Q2W	IXE80Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	23	20	24
Units: score on a scale				
least squares mean (standard error)	-1.7 (± 0.55)	-2.7 (± 0.53)	-2.7 (± 0.57)	-3.6 (± 0.53)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (PBO) v Adalimumab
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.166
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.76

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo (PBO) v IXE80Q4W
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.11
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	-0.4
Variability estimate	Standard error of the mean
Dispersion value	0.73

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo (PBO) v IXE80Q2W
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.182
Method	Mixed models analysis
Parameter estimate	LSMean Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.77

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 (DVUs) of the spine (from C2 to S1) are scored for bone marrow edema. A single DVU has a scoring range of 0 to 18, bringing the maximum total score to 414, with higher scores reflecting worse disease. Scoring was performed by central readers.
LSMean was calculated using ANCOVA model with treatment, geographic region, baseline CRP status and baseline value as fixed factors.

APD: All Randomized participants with baseline and week 16 SPARCC MRI score for spine.

End point type	Secondary

End point timeframe:

Baseline, Week 16

End point values	Placebo (PBO)	Adalimumab	IXE80Q2W	IXE80Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	81	82	76	78
Units: score on a scale				
least squares mean (standard error)	-1.51 (± 1.147)	-11.57 (± 1.113)	-9.58 (± 1.168)	-11.02 (± 1.160)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (PBO) v Adalimumab
Number of subjects included in analysis	163
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LSMean Difference
Point estimate	-10.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.2
upper limit	-6.9
Variability estimate	Standard error of the mean
Dispersion value	1.588

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo (PBO) v IXE80Q4W
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LSMean Difference
Point estimate	-9.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.6
upper limit	-6.4
Variability estimate	Standard error of the mean
Dispersion value	1.591

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo (PBO) v IXE80Q2W
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LSMean Difference
Point estimate	-8.08

Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.2
upper limit	-4.9
Variability estimate	Standard error of the mean
Dispersion value	1.603

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 76 Weeks

Adverse event reporting additional description:

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

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	IXE80Q4W-blinded treatment period
Reporting group description: -	
Reporting group title	IXE80Q2W-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	ADA-blinded treatment period
Reporting group description: -	
Reporting group title	IXE80Q4W/IXE80Q4W-extended treatment period
Reporting group description: -	
Reporting group title	PBO/IXE-extended treatment period
Reporting group description: -	
Reporting group title	ADA/PBO-washout treatment period
Reporting group description: -	
Reporting group title	ADA/PBO/IXE-extended treatment period
Reporting group description: -	
Reporting group title	IXE80Q2W-follow-up 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	IXE80Q4W-blinded treatment period	IXE80Q2W-blinded treatment period	PBO-blinded treatment period
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 81 (1.23%)	1 / 83 (1.20%)	0 / 86 (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)			

bladder cancer			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 81 (0.00%)	0 / 83 (0.00%)	0 / 86 (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
parathyroid tumour benign			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 81 (0.00%)	0 / 83 (0.00%)	0 / 86 (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
skin papilloma			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 81 (0.00%)	0 / 83 (0.00%)	0 / 86 (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 21.1			
subjects affected / exposed	0 / 81 (0.00%)	0 / 83 (0.00%)	0 / 86 (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			
ankle fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 81 (0.00%)	0 / 83 (0.00%)	0 / 86 (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
avulsion fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 81 (0.00%)	0 / 83 (0.00%)	0 / 86 (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
cervical vertebral fracture			

alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 81 (0.00%)	0 / 83 (0.00%)	0 / 86 (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
post procedural haematoma			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 81 (0.00%)	0 / 83 (0.00%)	0 / 86 (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
radius fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 81 (0.00%)	0 / 83 (0.00%)	0 / 86 (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
road traffic accident			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 81 (0.00%)	0 / 83 (0.00%)	0 / 86 (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			
atrioventricular block complete			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 81 (0.00%)	0 / 83 (0.00%)	0 / 86 (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			
cerebral haemorrhage			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 81 (0.00%)	0 / 83 (0.00%)	0 / 86 (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
subarachnoid haemorrhage			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 81 (0.00%)	0 / 83 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
lymphadenitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 81 (0.00%)	0 / 83 (0.00%)	0 / 86 (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
Reproductive system and breast disorders			
adnexal torsion			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[1]	0 / 13 (0.00%)	0 / 19 (0.00%)	0 / 15 (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			
crohn's disease			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 81 (0.00%)	1 / 83 (1.20%)	0 / 86 (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
dyspepsia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 81 (0.00%)	1 / 83 (1.20%)	0 / 86 (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
Skin and subcutaneous tissue disorders			
erythema multiforme			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 81 (0.00%)	1 / 83 (1.20%)	0 / 86 (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
Renal and urinary disorders			
nephrolithiasis			

alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 81 (0.00%)	0 / 83 (0.00%)	0 / 86 (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 21.1			
subjects affected / exposed	0 / 81 (0.00%)	0 / 83 (0.00%)	0 / 86 (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 21.1			
subjects affected / exposed	0 / 81 (0.00%)	0 / 83 (0.00%)	0 / 86 (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
plica syndrome			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 81 (0.00%)	0 / 83 (0.00%)	0 / 86 (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			
appendicitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 81 (0.00%)	0 / 83 (0.00%)	0 / 86 (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
cellulitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 81 (0.00%)	0 / 83 (0.00%)	0 / 86 (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
gastroenteritis			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 81 (0.00%)	1 / 83 (1.20%)	0 / 86 (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 haemophilus			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 81 (0.00%)	0 / 83 (0.00%)	0 / 86 (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
tonsillitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 81 (0.00%)	0 / 83 (0.00%)	0 / 86 (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 tract infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 81 (1.23%)	0 / 83 (0.00%)	0 / 86 (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

Serious adverse events	IXE80Q2W/IXE80Q2W-extended treatment period	ADA-blinded treatment period	IXE80Q4W/IXE80Q4W-extended treatment period
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 79 (3.80%)	3 / 90 (3.33%)	4 / 78 (5.13%)
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)			
bladder cancer			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 78 (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
parathyroid tumour benign			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 78 (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
skin papilloma			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 79 (1.27%)	0 / 90 (0.00%)	0 / 78 (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
Investigations			
blood creatine phosphokinase increased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
ankle fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 79 (0.00%)	1 / 90 (1.11%)	0 / 78 (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
avulsion fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 79 (1.27%)	0 / 90 (0.00%)	0 / 78 (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
cervical vertebral fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 78 (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
post procedural haematoma			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 78 (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
radius fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
road traffic accident			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	1 / 78 (1.28%)
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			
atrioventricular block complete			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 78 (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			
cerebral haemorrhage			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 78 (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
subarachnoid haemorrhage			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
lymphadenitis			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 78 (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
Reproductive system and breast disorders			
adnexal torsion			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[1]	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 13 (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			
crohn's disease			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 78 (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
dyspepsia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 78 (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
Skin and subcutaneous tissue disorders			
erythema multiforme			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 78 (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			
nephrolithiasis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 78 (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 21.1			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	1 / 78 (1.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
osteoarthritis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 78 (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
plica syndrome			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 79 (1.27%)	0 / 90 (0.00%)	0 / 78 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
appendicitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 79 (0.00%)	1 / 90 (1.11%)	0 / 78 (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
cellulitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 78 (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
gastroenteritis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 78 (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 haemophilus			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 78 (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
tonsillitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 79 (1.27%)	0 / 90 (0.00%)	0 / 78 (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
urinary tract infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 78 (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	PBO/IXE-extended treatment period	ADA/PBO-washout treatment period	ADA/PBO/IXE-extended treatment period
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 86 (4.65%)	0 / 88 (0.00%)	7 / 86 (8.14%)
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)			
bladder cancer			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 86 (0.00%)	0 / 88 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
parathyroid tumour benign			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 86 (0.00%)	0 / 88 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
skin papilloma			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 86 (0.00%)	0 / 88 (0.00%)	0 / 86 (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 21.1			
subjects affected / exposed	0 / 86 (0.00%)	0 / 88 (0.00%)	0 / 86 (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			
ankle fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 86 (0.00%)	0 / 88 (0.00%)	0 / 86 (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
avulsion fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 86 (0.00%)	0 / 88 (0.00%)	0 / 86 (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
cervical vertebral fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 86 (1.16%)	0 / 88 (0.00%)	0 / 86 (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
post procedural haematoma			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 86 (0.00%)	0 / 88 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
radius fracture			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 86 (0.00%)	0 / 88 (0.00%)	0 / 86 (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
road traffic accident			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 86 (0.00%)	0 / 88 (0.00%)	0 / 86 (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			
atrioventricular block complete			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 86 (1.16%)	0 / 88 (0.00%)	0 / 86 (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			
cerebral haemorrhage			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 86 (0.00%)	0 / 88 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
subarachnoid haemorrhage			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 86 (0.00%)	0 / 88 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
lymphadenitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 86 (1.16%)	0 / 88 (0.00%)	0 / 86 (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
Reproductive system and breast disorders			
adnexal torsion			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed[1]	0 / 15 (0.00%)	0 / 17 (0.00%)	0 / 16 (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			
crohn's disease			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 86 (0.00%)	0 / 88 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
dyspepsia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 86 (0.00%)	0 / 88 (0.00%)	0 / 86 (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
Skin and subcutaneous tissue disorders			
erythema multiforme			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 86 (0.00%)	0 / 88 (0.00%)	0 / 86 (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			
nephrolithiasis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 86 (0.00%)	0 / 88 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
arthritis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 86 (0.00%)	0 / 88 (0.00%)	0 / 86 (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 21.1			

subjects affected / exposed	1 / 86 (1.16%)	0 / 88 (0.00%)	0 / 86 (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
plica syndrome			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 86 (0.00%)	0 / 88 (0.00%)	0 / 86 (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			
appendicitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 86 (0.00%)	0 / 88 (0.00%)	0 / 86 (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
cellulitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 86 (1.16%)	0 / 88 (0.00%)	0 / 86 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastroenteritis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 86 (0.00%)	0 / 88 (0.00%)	0 / 86 (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 haemophilus			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 86 (0.00%)	0 / 88 (0.00%)	1 / 86 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
tonsillitis			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 86 (0.00%)	0 / 88 (0.00%)	0 / 86 (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 tract infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 86 (0.00%)	0 / 88 (0.00%)	0 / 86 (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-follow-up period	IXE80Q4W-follow-up period	PBO-follow-up period
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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)			
bladder cancer			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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
parathyroid tumour benign			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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
skin papilloma			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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 21.1			

subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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			
ankle fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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
avulsion fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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
cervical vertebral fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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
post procedural haematoma			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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
radius fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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
road traffic accident			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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			
atrioventricular block complete			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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			
cerebral haemorrhage			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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
subarachnoid haemorrhage			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
lymphadenitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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
Reproductive system and breast disorders			
adnexal torsion			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[1]	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 1 (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			
crohn's disease			

alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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
dyspepsia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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
Skin and subcutaneous tissue disorders			
erythema multiforme			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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			
nephrolithiasis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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
plica syndrome			

alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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			
appendicitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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
cellulitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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
gastroenteritis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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 haemophilus			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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
tonsillitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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 tract infection			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (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

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Gender specific adverse event, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.

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

Non-serious adverse events	IXE80Q4W-blinded treatment period	IXE80Q2W-blinded treatment period	PBO-blinded treatment period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 81 (13.58%)	18 / 83 (21.69%)	12 / 86 (13.95%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
uterine leiomyoma			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[2]	0 / 13 (0.00%)	0 / 19 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
injection site reaction			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 81 (0.00%)	7 / 83 (8.43%)	2 / 86 (2.33%)
occurrences (all)	0	37	33
Eye disorders			
ocular discomfort			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 81 (0.00%)	0 / 83 (0.00%)	0 / 86 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
adnexal torsion			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[3]	0 / 13 (0.00%)	0 / 19 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
menopausal symptoms			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[4]	0 / 13 (0.00%)	0 / 19 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

menstruation irregular			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[5]	0 / 13 (0.00%)	0 / 19 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
diarrhoea			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 81 (0.00%)	2 / 83 (2.41%)	2 / 86 (2.33%)
occurrences (all)	0	2	2
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 81 (0.00%)	1 / 83 (1.20%)	1 / 86 (1.16%)
occurrences (all)	0	1	1
Infections and infestations			
nasopharyngitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	6 / 81 (7.41%)	5 / 83 (6.02%)	6 / 86 (6.98%)
occurrences (all)	6	6	6
upper respiratory tract infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	7 / 81 (8.64%)	4 / 83 (4.82%)	4 / 86 (4.65%)
occurrences (all)	8	4	5
vaginal infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[6]	0 / 13 (0.00%)	0 / 19 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	IXE80Q2W/IXE80Q2W-extended treatment period	ADA-blinded treatment period	IXE80Q4W/IXE80Q4W-extended treatment period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 79 (26.58%)	16 / 90 (17.78%)	14 / 78 (17.95%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
uterine leiomyoma			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed[2]	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
injection site reaction			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	6 / 79 (7.59%)	3 / 90 (3.33%)	3 / 78 (3.85%)
occurrences (all)	34	6	4
Eye disorders			
ocular discomfort			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 79 (0.00%)	0 / 90 (0.00%)	0 / 78 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
adnexal torsion			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[3]	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
menopausal symptoms			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[4]	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
menstruation irregular			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[5]	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
diarrhoea			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	4 / 79 (5.06%)	4 / 90 (4.44%)	2 / 78 (2.56%)
occurrences (all)	4	4	2
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 79 (1.27%)	1 / 90 (1.11%)	3 / 78 (3.85%)
occurrences (all)	1	1	3
Infections and infestations			
nasopharyngitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	7 / 79 (8.86%)	6 / 90 (6.67%)	8 / 78 (10.26%)
occurrences (all)	9	7	8
upper respiratory tract infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	8 / 79 (10.13%)	2 / 90 (2.22%)	4 / 78 (5.13%)
occurrences (all)	9	3	4
vaginal infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[6]	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 13 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	PBO/IXE-extended treatment period	ADA/PBO-washout treatment period	ADA/PBO/IXE-extended treatment period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 86 (30.23%)	8 / 88 (9.09%)	20 / 86 (23.26%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
uterine leiomyoma			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[2]	0 / 15 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
injection site reaction			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	8 / 86 (9.30%)	0 / 88 (0.00%)	8 / 86 (9.30%)
occurrences (all)	53	0	24
Eye disorders			
ocular discomfort			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 86 (0.00%)	0 / 88 (0.00%)	0 / 86 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast			

disorders			
adnexal torsion			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[3]	0 / 15 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
menopausal symptoms			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[4]	0 / 15 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
menstruation irregular			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[5]	0 / 15 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
diarrhoea			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 86 (0.00%)	0 / 88 (0.00%)	1 / 86 (1.16%)
occurrences (all)	0	0	4
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 86 (0.00%)	0 / 88 (0.00%)	1 / 86 (1.16%)
occurrences (all)	0	0	1
Infections and infestations			
nasopharyngitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	17 / 86 (19.77%)	6 / 88 (6.82%)	7 / 86 (8.14%)
occurrences (all)	22	6	8
upper respiratory tract infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	4 / 86 (4.65%)	2 / 88 (2.27%)	4 / 86 (4.65%)
occurrences (all)	4	2	5
vaginal infection			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed[6]	0 / 15 (0.00%)	0 / 17 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	IXE80Q2W-follow-up period	IXE80Q4W-follow-up period	PBO-follow-up period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 24 (8.33%)	2 / 16 (12.50%)	1 / 1 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
uterine leiomyoma			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[2]	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
injection site reaction			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
ocular discomfort			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
adnexal torsion			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[3]	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
menopausal symptoms			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[4]	0 / 9 (0.00%)	0 / 3 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
menstruation irregular			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[5]	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

diarrhoea			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	2 / 16 (12.50%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
nasopharyngitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 24 (0.00%)	0 / 16 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
upper respiratory tract infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 24 (4.17%)	0 / 16 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
vaginal infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed[6]	0 / 9 (0.00%)	0 / 3 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0

Notes:

[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: Gender specific adverse event, 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: Gender specific adverse event, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.

[4] - 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: Gender specific adverse event, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.

[5] - 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: Gender specific adverse event, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.

[6] - 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: Gender specific adverse event, 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? Yes

Date	Amendment
23 December 2016	To remove specific limitation of enrolling equal numbers of participants with elevated/non-elevated CRP such that all patients who meet protocol eligibility criteria can be enrolled independent of having elevated or nonelevated CRP.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported