



Clinical trial results:

A Phase 3, Multicenter Study with a 36-Week Open-Label Period Followed by a Randomized Double-Blind Withdrawal Period from Week 36 to Week 104 to Evaluate the Long Term Efficacy and Safety of Ixekizumab (LY2439821) 80 mg Every 2 Weeks in Biologic Disease-Modifying Antirheumatic Drug-Naive Patients with Active Psoriatic Arthritis

Summary

EudraCT number	2015-002433-22
Trial protocol	SK EE CZ GB ES BG PL
Global end of trial date	30 October 2018

Results information

Result version number	v1 (current)
This version publication date	11 November 2019
First version publication date	11 November 2019

Trial information

Trial identification

Sponsor protocol code	I1F-MC-RHBF
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02584855
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 14518

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

Global end of trial reached?	Yes
Global end of trial date	30 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 long-term efficacy of ixekizumab compared to placebo in participants with active psoriatic arthritis.

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	18 November 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Czech Republic: 90
Country: Number of subjects enrolled	United States: 32
Country: Number of subjects enrolled	Ukraine: 43
Country: Number of subjects enrolled	Poland: 60
Country: Number of subjects enrolled	Mexico: 16
Country: Number of subjects enrolled	South Africa: 26
Country: Number of subjects enrolled	United Kingdom: 23
Country: Number of subjects enrolled	Slovakia: 16
Country: Number of subjects enrolled	Bulgaria: 20
Country: Number of subjects enrolled	Estonia: 47
Country: Number of subjects enrolled	Russian Federation: 10
Country: Number of subjects enrolled	Spain: 11
Worldwide total number of subjects	394
EEA total number of subjects	267

Notes:

Subjects enrolled per age group

In utero	0
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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)	371
From 65 to 84 years	23
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study had four periods: Period 1: Screening period lasting from 4 to 30 days before Week 0, Period 2: Initial open-label treatment period from Week 0 up to Week 36, Period 3: randomized double-blind withdrawal period from Week 36 to week 104 (or, early termination or relapse) and Period 4: post treatment follow-up.

Pre-assignment

Screening details:

Participants were randomized during week 36 to week 64. The criteria for randomization in period 3 was having received ixekizumab (IXE) 80 mg Q2W for at least 6 months and meeting Coates criteria for minimal disease activity (MDA) for 3 consecutive months over 4 consecutive visits. The criteria was met anytime from 36 to 64 weeks.

Period 1

Period 1 title	Open-Label Treatment Period
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Ixekizumab Open Label
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Arm description:

Open-Label Treatment Period (OLTP): Starting dose of 160 milligrams (mg) ixekizumab given as two subcutaneous (SC) injections at baseline (Week 0) followed by 80 mg given as one SC injection every two weeks (Q2W) from week 2 to randomization (week 36 to 64).

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

Dosage and administration details:

160 milligrams (mg) ixekizumab given as two subcutaneous (SC) injections at baseline (Week 0) followed by 80 mg given as one SC injection every two weeks (Q2W) from week 2 to randomization (week 36 to 64).

Number of subjects in period 1	Ixekizumab Open Label
Started	394
Received at least one dose of study drug	394
Met randomization Criteria	158 ^[1]
Non-randomized	133 ^[2]
Completed	291
Not completed	103
Consent withdrawn by subject	21
Adverse event, non-fatal	14
Death	2

No PI Available	2
Sponsor Decision	1
Lost to follow-up	1
Lack of efficacy	61
Protocol deviation	1

Notes:

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

Justification: The reason why randomized + non randomized do not sum up to the total entered participants is because 103 participants discontinued open label treatment.

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

Justification: The reason why randomized + non randomized do not sum up to the total entered participants is because 103 participants discontinued open label treatment.

Period 2

Period 2 title	Double-Blind Withdrawal 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	IXE80Q2W Non-randomized

Arm description:

Participants completed open label but did not meet criteria for randomization to the double-blind Withdrawal Period.

Participants continued to receive 80 mg given as one SC injection every two weeks during the double-blind withdrawal period.

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

Dosage and administration details:

80 mg given as one SC injection every two weeks during the double-blind withdrawal period.

Arm title	Ixekizumab
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Arm description:

Participants completed open label and met criteria for randomization to the double-blind Withdrawal Period.

Double-Blind Withdrawal Period: 80 mg ixekizumab given as one SC injection Q2W from randomization to week 104 (or, early termination or relapse).

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

Dosage and administration details:

80 mg ixekizumab given as one SC injection Q2W from randomization to week 104 (or, early termination or relapse).

Arm title	Placebo
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Arm description:

Participants completed open label and met criteria for randomization to the double-blind Withdrawal Period.

Double-Blind Withdrawal Period: Placebo given as one SC injection Q2W any time from randomization to week 104 (or, early termination or relapse)

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

Dosage and administration details:

Placebo given as one SC injection Q2W any time from randomization to week 104 (or, early termination or relapse)

Number of subjects in period 2	IXE80Q2W Non-randomized	Ixekizumab	Placebo
Started	133	79	79
Relapsed	0 ^[3]	67 ^[4]	30 ^[5]
Completed	118	77	78
Not completed	15	2	1
Consent withdrawn by subject	-	2	-
Adverse event, non-fatal	4	-	1
Declined Transfer to a Different Site	1	-	-
Lack of efficacy	10	-	-

Notes:

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

Justification: The reason why randomized + non randomized do not sum up to the total entered participants is because 103 participants discontinued open label treatment.

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

Justification: The reason why randomized + non randomized do not sum up to the total entered participants is because 103 participants discontinued open label treatment.

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

Justification: The reason why randomized + non randomized do not sum up to the total entered participants is because 103 participants discontinued open label treatment.

Period 3

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

Arms

Are arms mutually exclusive?	No
Arm title	IXE80Q2W Post-Treatment Follow-up Period

Arm description:

Participants did not receive any study treatment during post treatment follow-up period. Post-Treatment Follow-up Period was summarized by last treatment assigned to a participant prior to entering the post-treatment follow up period.

Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Placebo Post-Treatment Follow-up Period

Arm description:

Participants did not receive any study treatment during post treatment follow-up period. Placebo Post-Treatment Follow-up Period was summarized by last treatment assigned to a participant prior to entering the post-treatment follow up period.

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 3	IXE80Q2W Post-Treatment Follow-up Period	Placebo Post-Treatment Follow-up Period
Started	355	12
Completed	347	12
Not completed	8	0
Consent withdrawn by subject	7	-
Protocol deviation	1	-

Baseline characteristics

Reporting groups

Reporting group title	Open-Label Treatment Period
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Reporting group description: -

Reporting group values	Open-Label Treatment Period	Total	
Number of subjects	394	394	
Age categorical			
Units: Subjects			

Age continuous			
All participants who received at least one dose of study drug.			
Units: years			
arithmetic mean	47.4		
standard deviation	± 11.40	-	
Gender categorical			
Units: Subjects			
Female	212	212	
Male	182	182	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	16	16	
Not Hispanic or Latino	330	330	
Unknown or Not Reported	48	48	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	6	6	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	1	1	
White	385	385	
More than one race	2	2	
Unknown or Not Reported	0	0	
Region of Enrollment			
Units: Subjects			
United States	32	32	
Czechia	90	90	
Ukraine	43	43	
Poland	60	60	
Mexico	16	16	
South Africa	26	26	
United Kingdom	23	23	
Slovakia	16	16	
Bulgaria	20	20	
Estonia	47	47	
Russia	10	10	
Spain	11	11	

End points

End points reporting groups

Reporting group title	Ixekizumab Open Label
Reporting group description: Open-Label Treatment Period (OLTP): Starting dose of 160 milligrams (mg) ixekizumab given as two subcutaneous (SC) injections at baseline (Week 0) followed by 80 mg given as one SC injection every two weeks (Q2W) from week 2 to randomization (week 36 to 64).	
Reporting group title	IXE80Q2W Non-randomized
Reporting group description: Participants completed open label but did not meet criteria for randomization to the double-blind Withdrawal Period. Participants continued to receive 80 mg given as one SC injection every two weeks during the double-blind withdrawal period.	
Reporting group title	Ixekizumab
Reporting group description: Participants completed open label and met criteria for randomization to the double-blind Withdrawal Period. Double-Blind Withdrawal Period: 80 mg ixekizumab given as one SC injection Q2W from randomization to week 104 (or, early termination or relapse).	
Reporting group title	Placebo
Reporting group description: Participants completed open label and met criteria for randomization to the double-blind Withdrawal Period. Double-Blind Withdrawal Period: Placebo given as one SC injection Q2W any time from randomization to week 104 (or, early termination or relapse)	
Reporting group title	IXE80Q2W Post-Treatment Follow-up Period
Reporting group description: Participants did not receive any study treatment during post treatment follow-up period. Post-Treatment Follow-up Period was summarized by last treatment assigned to a participant prior to entering the post-treatment follow up period.	
Reporting group title	Placebo Post-Treatment Follow-up Period
Reporting group description: Participants did not receive any study treatment during post treatment follow-up period. Placebo Post-Treatment Follow-up Period was summarized by last treatment assigned to a participant prior to entering the post-treatment follow up period.	

Primary: Double-Blind Withdrawal Period: Time to Relapse (No Longer Meeting Coates Criteria for Minimal Disease Activity [MDA])

End point title	Double-Blind Withdrawal Period: Time to Relapse (No Longer Meeting Coates Criteria for Minimal Disease Activity [MDA])
End point description: Relapse is loss of MDA response. MDA is achieved if 5 of 7 outcome measures are fulfilled: TJC ≤ 1 ; SJC ≤ 1 ; psoriasis activity & severity index (PASI total score) ≤ 1 or body surface area (BSA) ≤ 3 ; participant pain VAS score of ≤ 15 ; participant global disease activity VAS score of ≤ 20 ; HAQ-DI score ≤ 0.5 ; and tender entheseal points ≤ 1 . Participants met the randomization criteria if they had MDA for 3 consecutive months over 4 consecutive visits. Time-to relapse was calculated in weeks as follows: ((Date of Relapse) - Date of first injection of randomized study treatment in period 3) + 1 divided by 7. If the date of first dose is missing, the date of randomization will be used. Participants completing Period 3 will be censored at date of completion (the date of the last scheduled visit in the period). Participants without a date of completion or discontinuation for Period 3 will be censored at latest non-missing date out of the following dates: date of last dose & date of last attended visit in Period 3.	
End point type	Primary

End point timeframe:

Double Blind Randomization through Week 104 (or Early Termination or Relapse)

APD: All participants who received at least one dose of study drug in randomized withdrawal Intent-to-Treat population. Censored participants were Ixekizumab=49 and Placebo=12.

End point values	Ixekizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79 ^[1]	79		
Units: Weeks				
median (confidence interval 95%)	9999 (64.29 to 9999)	22.29 (16.14 to 28.29)		

Notes:

[1] - 9999=NA

Median and upper CI not be estimated due to insufficient events in analysis duration.

Statistical analyses

Statistical analysis title	Time to Relapse
Statistical analysis description: Log Rank Test adjusting for geographic region and conventional disease-modifying antirheumatic drug (cDMARD) use at the time of double blind randomization.	
Comparison groups	Ixekizumab v Placebo
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logrank

Secondary: Double-Blind Withdrawal Period: Percentage of Participants Who Relapse in MDA

End point title	Double-Blind Withdrawal Period: Percentage of Participants Who Relapse in MDA
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End point description:

Relapsed participants are defined as participants no longer meeting Coates criteria for MDA. MDA is achieved if 5 of 7 outcome measures are fulfilled: TJC ≤ 1 ; SJC ≤ 1 ; psoriasis activity and severity index (PASI total score) ≤ 1 or body surface area (BSA) ≤ 3 ; participant pain VAS score of ≤ 15 ; participant global disease activity VAS score of ≤ 20 ; HAQ-DI score ≤ 0.5 ; and tender enthesal points ≤ 1 .

End point type	Secondary
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End point timeframe:

Double Blind Randomization through Week 104 (or Early Termination or Relapse)

Analysis Population Description (APD): All participants who received at least one dose of study drug in randomized withdrawal Intent-to-Treat population.

End point values	Ixekizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	79		
Units: percentage of participants				
number (confidence interval 95%)	40.5 (29.7 to 51.3)	86.1 (78.4 to 93.7)		

Statistical analyses

Statistical analysis title	Percentage of Participants Who Relapse in MDA
Statistical analysis description:	
Logistic regression adjusting for treatment, geographic region, and cDMARD use at the time of double-blind randomization .	
Comparison groups	Ixekizumab v Placebo
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	-45.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-58.8
upper limit	-32.3

Secondary: Double-Blind Withdrawal Period: Time to Loss of Response in Each Individual Component of MDA: Tender Joint Count 68 (TJC)

End point title	Double-Blind Withdrawal Period: Time to Loss of Response in Each Individual Component of MDA: Tender Joint Count 68 (TJC)
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End point description:

TJC is the number of tender and painful joints determined for each participant by examination of 68 joints. TJC possible values range from 0 to 68. A lower TJC indicated less number of joints with tenderness. A higher TJC indicated more joint tenderness. Joints were assessed by pressure and joint manipulation on physical examination. Participants were asked for pain sensations on these manipulations and watched for spontaneous pain reactions. Any positive response on pressure, movement, or both was translated into a single tender-versus-nontender dichotomy.

Loss of Response = Not Meeting less than or equal to 1 TJC.

Time to loss of response (in weeks) = (date of loss of response - date of first injection of randomized dose of study treatment in the Randomized Double-Blind Withdrawal Period + 1)/7.

Censored participants: Ixekizumab= 29 and Placebo= 16.

End point type	Secondary
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End point timeframe:

Double Blind Randomization through Week 104 (or Early Termination or Relapse)

All participants who received at least 1 dose of study drug in the randomized withdrawal Intent-to-Treat Population who had tender joint counts ≤ 1 at time of randomization.

End point values	Ixekizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56 ^[2]	57		
Units: weeks				
median (confidence interval 95%)	64.29 (24.14 to 9999)	22.29 (12.29 to 28.71)		

Notes:

[2] - 9999=NA. Upper CI could not be estimated due to insufficient events in analysis duration.

Statistical analyses

No statistical analyses for this end point

Secondary: Double-Blind Withdrawal Period: Time to Loss of Response in Each Individual Component of MDA: Swollen Joint Count 66 (SJC)

End point title	Double-Blind Withdrawal Period: Time to Loss of Response in Each Individual Component of MDA: Swollen Joint Count 66 (SJC)
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End point description:

SJC is the number of swollen joints determined for each participant by examination of 66 joints. SJC possible values range from 0 to 66. A lower SJC indicated less joints with swelling. A higher SJC indicated more joints with swelling. Swelling was defined as palpable fluctuating synovitis of the joint. Loss of Response = Not Meeting less than or equal to 1 SJC.

Time to loss of response (in weeks) = (date of loss of response - date of first injection of randomized dose of study treatment in the Randomized Double-Blind Withdrawal Period + 1)/7.

Analysis Population Description: All participants who received at least one dose of study drug in the randomized withdrawal Intent-to-Treat population who had swollen joint counts ≤ 1 at time of randomization. Censored participants: Ixekizumab= 61 and Placebo = 40.

End point type	Secondary
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End point timeframe:

Double Blind Randomization through Week 104 (or Early Termination or Relapse).

End point values	Ixekizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72 ^[3]	73 ^[4]		
Units: weeks				
median (confidence interval 95%)	9999 (9999 to 9999)	28.71 (20.14 to 9999)		

Notes:

[3] - 9999=NA Median and CI could not be estimated due to insufficient events in analysis duration.

[4] - 9999=NA. Upper CI could not be estimated due to insufficient events in analysis duration.

Statistical analyses

No statistical analyses for this end point

Secondary: Double-Blind Withdrawal Period: Time to Loss of Response in Each Individual Component of MDA: Psoriasis Area and Severity Index (PASI)

End point title	Double-Blind Withdrawal Period: Time to Loss of Response in Each Individual Component of MDA: Psoriasis Area and Severity Index (PASI)
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End point description:

The PASI is an index that combines assessments of the extent of body-surface involvement in 4 anatomical regions (head, trunk, arms, and legs) and the severity of desquamation, erythema, and plaque induration/infiltration (thickness) in each region, yielding an overall score of 0 for no psoriasis to 72 for the most severe disease.

Loss of Response = Not Meeting less than or equal to 1 PASI total score.

Time to loss of response (in weeks) = (date of loss of response - date of first injection of randomized dose of study treatment in the Randomized Double-Blind Withdrawal Period + 1)/7.

Analysis Population Description: All participants who received at least one dose of study drug in the randomized withdrawal intent-to-treat population Who had PASI ≤ 1 at time of randomization.

Censored participants: Ixekizumab = 64 and Placebo = 43.

End point type	Secondary
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End point timeframe:

Double Blind Randomization through Week 104 (or Early Termination or Relapse)

End point values	Ixekizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73 ^[5]	77		
Units: weeks				
median (confidence interval 95%)	9999 (9999 to 9999)	36.00 (24.14 to 48.14)		

Notes:

[5] - 9999=NA. Median and CI could not be estimated due to insufficient events in analysis duration.

Statistical analyses

Statistical analysis title	Time to Loss of Response (PASI)
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Statistical analysis description:

Log Rank Test adjusting for geographic region and cDMARD use at the time of double blind randomization.

Comparison groups	Ixekizumab v Placebo
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logrank

Secondary: Double-Blind Withdrawal Period: Time to Loss of Response in Each Individual Component of MDA: BSA

End point title	Double-Blind Withdrawal Period: Time to Loss of Response in Each Individual Component of MDA: BSA
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End point description:

BSA is an investigator evaluated measure, where the percentage of involvement of psoriasis on each participant's BSA is assessed. BSA was measured on a continuous scale from 0% = no involvement to

100% = full involvement, where 1% corresponded to the size of the participant's handprint including the palm, fingers, and thumb. Loss of Response = Not meeting less than or equal to 3% BSA.

Time to loss of response (in weeks) = (date of loss of response - date of first injection of randomized dose of study treatment in the Randomized Double-Blind Withdrawal Period + 1)/7.

Analysis Population Description: All participants who received at least one dose of study drug in the randomized Withdrawal Intent-to-Treat Population who had BSA ≤ 3% at time of randomization.

Censored participants: Ixekizumab=70 and Placebo= 59.

End point type	Secondary
End point timeframe:	
Double Blind Randomization through Week 104 (or Early Termination or Relapse)	

End point values	Ixekizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73 ^[6]	78 ^[7]		
Units: weeks				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (36.00 to 9999)		

Notes:

[6] - 9999=NA. Median and CI could not be estimated due to insufficient events in analysis duration.

[7] - 9999=NA. Confidence Interval could not be estimated due to insufficient events in analysis duration.

Statistical analyses

Statistical analysis title	Time to Loss of Response (BSA)
Statistical analysis description:	
Log Rank Test adjusting for geographic region and cDMARD use at the time of double blind randomization.	
Comparison groups	Ixekizumab v Placebo
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logrank

Secondary: Double-Blind Withdrawal Period: Time to Loss of Response in Each Individual Component of MDA: Pain Visual Analog Scale (VAS) Score

End point title	Double-Blind Withdrawal Period: Time to Loss of Response in Each Individual Component of MDA: Pain Visual Analog Scale (VAS) Score
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End point description:

The pain VAS is an instrument used to measure a person's subjective quantitative evaluation of an item such as pain intensity. The VAS contains a continuous line between two endpoints whereby the respondent places a mark on the line to indicate his or her response. The scale ranges from 0 (no pain) to 100 (unbearable pain). The scores were measured to the nearest millimeter from the left. Loss of Response = Not Meeting less than or equal to 15 Pain VAS. Time to loss of response (in weeks) = (date of loss of response - date of first injection of randomized dose of study treatment in the Randomized Double-Blind Withdrawal Period + 1)/7.

Analysis Population Description: All participants who received at least one dose of study drug in the randomized withdrawal Intent-to-Treat Population who had Pain VAS ≤ 15 at time of randomization.

Censored participants: Ixekizumab=42 and Placebo= 7.

End point type	Secondary
End point timeframe:	
Double Blind Randomization through Week 104 (or Early Termination or Relapse)	

End point values	Ixekizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72 ^[8]	68		
Units: weeks				
median (confidence interval 95%)	9999 (36.14 to 9999)	16.14 (12.14 to 22.71)		

Notes:

[8] - 9999=NA. Confidence Interval could not be estimated due to insufficient events in analysis duration.

Statistical analyses

Statistical analysis title	Time to Loss of Response VAS Score
Statistical analysis description:	
Log Rank Test adjusting for geographic region and cDMARD use at the time of double blind randomization.	
Comparison groups	Ixekizumab v Placebo
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logrank

Secondary: Double-Blind Withdrawal Period: Time to Loss of Response in Each Individual Component of MDA: Patients Global Assessment of Disease Activity (PatGA) Visual Analog Scale (VAS) score

End point title	Double-Blind Withdrawal Period: Time to Loss of Response in Each Individual Component of MDA: Patients Global Assessment of Disease Activity (PatGA) Visual Analog Scale (VAS) score
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End point description:

Participants scored their overall assessment of their psoriatic arthritis (PsA) activity on a 0 to 100 mm horizontal VAS. The scale ranged from 0 (no disease activity) to 100 (extremely active disease activity). The scores were measured to the nearest millimeter from the left.

Loss of Response = Not Meeting less than or equal to 20 PatGA.

Time to loss of response (in weeks) = (date of loss of response - date of first injection of randomized dose of study treatment in the Randomized Double-Blind Withdrawal Period + 1)/7.

Analysis Population Description: All participants who received at least one dose of study drug in the randomized withdrawal Intent-to-Treat population Who had PatGA VAS ≤ 20 at time of randomization. Censored participants: Ixekizumab= 57 and Placebo=18.

End point type	Secondary
End point timeframe:	
Double Blind Randomization through Week 104 (or Early Termination or Relapse)	

End point values	Ixekizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77 ^[9]	74		
Units: weeks				
median (confidence interval 95%)	9999 (9999 to 9999)	20.57 (16.14 to 28.14)		

Notes:

[9] - 9999=NA. Median and CI could not be estimated due to insufficient events in analysis duration.

Statistical analyses

Statistical analysis title	Time to Loss of Response (PatGA and VAS Score)
Statistical analysis description:	
Log Rank Test adjusting for geographic region and cDMARD use at the time of double blind randomization.	
Comparison groups	Ixekizumab v Placebo
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logrank

Secondary: Double-Blind Withdrawal Period: Time to Loss of Response in Each Individual Component of MDA: Health Assessment Questionnaire-Disability Index (HAQ-DI)

End point title	Double-Blind Withdrawal Period: Time to Loss of Response in Each Individual Component of MDA: Health Assessment Questionnaire-Disability Index (HAQ-DI)
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End point description:

The HAQ-DI questionnaire assesses the participant's self-perception on the degree of difficulty [0 (without any difficulty), 1 (with some difficulty), 2 (with much difficulty), and 3 (unable to do)] when dressing and grooming, arising, eating, walking, hygiene, reaching, gripping, and performing other daily activities. Scores for each functional area were averaged to calculate HAQ-DI scores, which ranged from 0 (no disability) to 3 (severe disability). A decrease in HAQ-DI score indicated an improvement in the participant's condition.

Loss of Response = Not Meeting less than or equal to 0.5 HAQ-DI.

Time to loss of response (in weeks) = (date of loss of response - date of first injection of randomized dose of study treatment in the Randomized

Double-Blind Withdrawal Period + 1)/7.

Censored participants: Ixekizumab= 55 and Placebo=53.

End point type	Secondary
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End point timeframe:

Double Blind Randomization through Week 104 (or Early Termination or Relapse)

All participants who received at least one dose of study drug in the randomized withdrawal Intent-to-Treat population Who had HAQ-DI ≤ 0.5 at Time of randomization.

End point values	Ixekizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69 ^[10]	68 ^[11]		
Units: weeks				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (48.14 to 9999)		

Notes:

[10] - 9999=NA. Median and CI could not be estimated due to insufficient events in analysis duration.

[11] - 9999=NA. Median and Upper CI could not be estimated due to insufficient events in analysis duration.

Statistical analyses

Statistical analysis title	Time to Loss of Response (HAQ-DI)
Statistical analysis description:	
Log Rank Test adjusting for geographic region and cDMARD use at the time of double blind randomization.	
Comparison groups	Ixekizumab v Placebo
Number of subjects included in analysis	137
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logrank

Secondary: Double-Blind Withdrawal Period: Time to Loss of Response in Each Individual Component of MDA: Tender Enthesesal Points

End point title	Double-Blind Withdrawal Period: Time to Loss of Response in Each Individual Component of MDA: Tender Enthesesal Points
End point description:	
Tender enthesesal points was based on the assessment of the 18 enthesesal points. Loss of Response = Not Meeting less than or equal to 1 Tender Enthesesal Point. Time to loss of response (in weeks) = (date of loss of response - date of first injection of randomized dose of study treatment in the Randomized Double-Blind Withdrawal Period + 1)/7.	
Analysis Population Description: All participants who received at least one dose of study drug in the randomized withdrawal Intent-to-Treat Population who had tender Enthesesal Point ≤ 1 at time of randomization. Censored participants: Ixekizumab= 58 and Placebo= 58.	
End point type	Secondary
End point timeframe:	
Double Blind Randomization through Week 104 (or Early Termination or Relapse)	

End point values	Ixekizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73 ^[12]	72 ^[13]		
Units: weeks				
median (confidence interval 95%)	9999 (999 to 9999)	9999 (60.29 to 9999)		

Notes:

[12] - 9999=NA. Median and CI could not be estimated due to insufficient events in analysis duration.

[13] - 9999=NA. Median and CI could not be estimated due to insufficient events in analysis duration.

Statistical analyses

No statistical analyses for this end point

Secondary: Open-Label Treatment Period: Time to Achieve Randomization Criteria (Meeting MDA for 3 Consecutive Months over 4 Consecutive Visits)

End point title	Open-Label Treatment Period: Time to Achieve Randomization Criteria (Meeting MDA for 3 Consecutive Months over 4 Consecutive Visits)
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End point description:

Time to meeting MDA for 3 Consecutive Months Over 4 Consecutive Visits. Time to first response (in weeks) = [(date of first response - date of first injection of study treatment in the Open-Label Treatment Period)+1]/7.

Open-Label Treatment Period ended at the time when a participant was randomized so the end time was not the same for all participants. Participants were randomized only if they met randomization criteria which was at anytime from week 36 to week 64.

Analysis Population Description: All participants who received at least one dose of study drug in initial open-label treatment period. Censored participants were 239.

End point type	Secondary
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End point timeframe:

Open Label Baseline through Double-Blind Randomization (Week 36 to 64)

End point values	Ixekizumab Open Label			
Subject group type	Reporting group			
Number of subjects analysed	394 ^[14]			
Units: weeks				
median (confidence interval 95%)	64.43 (56.14 to 9999)			

Notes:

[14] - 9999=NA. Upper CI could not be estimated due to insufficient events in analysis duration.

Statistical analyses

No statistical analyses for this end point

Secondary: Double-Blind Withdrawal Period: Time to Re-Gain MDA Following Relapse in MDA

End point title	Double-Blind Withdrawal Period: Time to Re-Gain MDA Following Relapse in MDA
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End point description:

MDA is achieved if 5 of 7 outcome measures are fulfilled: TJC ≤ 1 ; SJC ≤ 1 ; psoriasis activity and severity index (PASI total score) ≤ 1 or BSA ≤ 3 ; participant pain VAS score of ≤ 15 ; participant global disease activity VAS score of ≤ 20 ; HAQ-DI score ≤ 0.5 ; and tender entheses points ≤ 1 . Time to first response (in weeks) = (date of first response - date of first injection of study treatment in the Relapse Period + 1)/7.

Analysis Population Description: All participants who received at least one dose of study drug and relapsed in MDA After Double Blind Randomization Until Re-Gain MDA. Censored participants were: Ixekizumab= 3 and Placebo= 3.

End point type	Secondary
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End point timeframe:

Relapse in MDA After Double Blind Randomization through Week 104 (or Early Termination)

End point values	Ixekizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	67		
Units: weeks				
median (confidence interval 95%)	4.71 (4.14 to 8.29)	4.14 (4.14 to 4.29)		

Statistical analyses

No statistical analyses for this end point

Secondary: Double-Blind Withdrawal Period: Change from Baseline in Physical Functioning Assessed by the Health Assessment Questionnaire-Disability Index (HAQ-DI)

End point title	Double-Blind Withdrawal Period: Change from Baseline in Physical Functioning Assessed by the Health Assessment Questionnaire-Disability Index (HAQ-DI)
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End point description:

The HAQ-DI questionnaire assesses the participant's self-perception on the degree of difficulty [0 (without any difficulty), 1 (with some difficulty), 2 (with much difficulty), and 3 (unable to do)] when dressing and grooming, arising, eating, walking, hygiene, reaching, gripping, and performing other daily activities. Scores for each functional area were averaged to calculate HAQ-DI scores, which ranged from 0 (no disability) to 3 (severe disability). A decrease in HAQ-DI score indicated an improvement in the participant's condition. Least Square (LS) mean calculated using Mixed Model Repeated Measurements (MMRM) analysis with treatment group, baseline measure, geographic region, cDMARD use, treatment week, baseline measure-by-treatment week interaction term, and treatment week-by-treatment interaction term as fixed factors.

Participants were randomized only if they met randomization criteria which was at anytime from week 36 to week 64.

End point type	Secondary
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End point timeframe:

Baseline, 40 Weeks from Double Blind Randomization (Week 36 to 64)

All participants who received at least one dose of study drug had a baseline and post baseline measure in the Double-Blind Withdrawal Period.

End point values	Ixekizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	22		
Units: score on a scale				
least squares mean (standard error)	-0.79 (\pm 0.06)	-0.67 (\pm 0.06)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up To 3 Years

Adverse event reporting additional description:

All participants who received at least one dose of study drug. Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.1
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Reporting groups

Reporting group title	Ixekizumab Open Label
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Reporting group description:

Open-Label Treatment Period: Starting dose of 160 milligrams (mg) ixekizumab given as two subcutaneous (SC) injections at baseline (week 0) followed by 80 mg given as one SC injection every two weeks (Q2W) from week 2 to randomization (week 36 to 64).

Reporting group title	Ixekizumab
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Reporting group description:

Participants completed open label and met criteria for randomization to the double-blind Withdrawal Period.

Double-Blind Withdrawal Period: 80 mg ixekizumab given as one SC injection Q2W from randomization to week 104 (or, early termination or relapse).

Reporting group title	Placebo
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Reporting group description:

Participants completed open label and met criteria for randomization to the double-blind Withdrawal Period.

Double-Blind Withdrawal Period: Placebo given as one SC injection Q2W any time from randomization to week 104 (or, early termination or relapse).

Reporting group title	IXE80Q2W Non-randomized Population to Withdrawal Period
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Reporting group description:

Participants completed open label but did not meet criteria for randomization to the double-blind Withdrawal Period.

Participants continued to receive 80 mg given as one SC injection every two weeks during the double-blind withdrawal period.

Reporting group title	IXE80Q2W Relapse Period
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Reporting group description:

IXE80Q2W Relapse Period

Double Blind Period: 80 mg ixekizumab given as one SC injection Q2W from randomization to week 104 (or, early termination or relapse).

Double Blind Period: Placebo given as one SC injection Q2W any time from randomization to week 104 (or, early termination or relapse).

Reporting group title	IXE80Q2W Post-Treatment Follow-up Period
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Reporting group description:

Participants did not receive any study treatment during post treatment follow-up period. Post-Treatment Follow-up Period was summarized by last treatment assigned to a participant prior to entering the post-treatment follow up period.

Reporting group title	Placebo Post-Treatment Follow-up Period
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Reporting group description:

Participants did not receive any study treatment during post treatment follow-up period. Placebo Post-Treatment Follow-up Period was summarized by last treatment assigned to a participant prior to

Serious adverse events	Ixekizumab Open Label	Ixekizumab	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 394 (5.08%)	1 / 79 (1.27%)	2 / 79 (2.53%)
number of deaths (all causes)	2	0	0
number of deaths resulting from adverse events	1	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
uterine leiomyoma			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed ^[1]	1 / 212 (0.47%)	0 / 32 (0.00%)	0 / 39 (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
General disorders and administration site conditions			
drowning			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 394 (0.25%)	0 / 79 (0.00%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
non-cardiac chest pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 394 (0.25%)	0 / 79 (0.00%)	0 / 79 (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
Reproductive system and breast disorders			
endometriosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed ^[2]	0 / 212 (0.00%)	1 / 32 (3.13%)	0 / 39 (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
ovarian cyst			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed ^[3]	0 / 212 (0.00%)	0 / 32 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
acute respiratory failure			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 394 (0.00%)	0 / 79 (0.00%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
respiratory failure			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 394 (0.25%)	0 / 79 (0.00%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
troponin increased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 394 (0.00%)	0 / 79 (0.00%)	0 / 79 (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			
fall			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 394 (0.00%)	0 / 79 (0.00%)	0 / 79 (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
foreign body in eye			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 394 (0.25%)	0 / 79 (0.00%)	0 / 79 (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
humerus fracture			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 394 (0.00%)	0 / 79 (0.00%)	0 / 79 (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
meniscus injury alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 394 (0.25%)	0 / 79 (0.00%)	0 / 79 (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
radius fracture alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 394 (0.00%)	0 / 79 (0.00%)	0 / 79 (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 / 394 (0.00%)	0 / 79 (0.00%)	0 / 79 (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
thermal burn alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 394 (0.25%)	0 / 79 (0.00%)	0 / 79 (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
upper limb fracture alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 394 (0.00%)	0 / 79 (0.00%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders acute myocardial infarction alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 394 (0.25%)	0 / 79 (0.00%)	0 / 79 (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
angina unstable			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 394 (0.25%)	0 / 79 (0.00%)	0 / 79 (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
coronary artery disease			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 394 (0.25%)	0 / 79 (0.00%)	0 / 79 (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			
embolic stroke			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 394 (0.25%)	0 / 79 (0.00%)	0 / 79 (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
transient ischaemic attack			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 394 (0.25%)	0 / 79 (0.00%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
vascular headache			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 394 (0.25%)	0 / 79 (0.00%)	0 / 79 (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
Gastrointestinal disorders			
crohn's disease			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 394 (0.25%)	0 / 79 (0.00%)	0 / 79 (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
gastritis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 394 (0.25%)	0 / 79 (0.00%)	0 / 79 (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
gastrointestinal necrosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 394 (0.25%)	0 / 79 (0.00%)	0 / 79 (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
intestinal obstruction			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 394 (0.25%)	0 / 79 (0.00%)	0 / 79 (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
large intestine polyp			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 394 (0.00%)	0 / 79 (0.00%)	1 / 79 (1.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
cholecystitis acute			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 394 (0.00%)	0 / 79 (0.00%)	0 / 79 (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
cholelithiasis			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	2 / 394 (0.51%)	0 / 79 (0.00%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hepatic steatosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 394 (0.00%)	0 / 79 (0.00%)	0 / 79 (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			
angioedema			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 394 (0.25%)	0 / 79 (0.00%)	0 / 79 (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
Musculoskeletal and connective tissue disorders			
foot deformity			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 394 (0.25%)	0 / 79 (0.00%)	0 / 79 (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
osteoarthritis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 394 (0.25%)	0 / 79 (0.00%)	0 / 79 (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			
bronchitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	2 / 394 (0.51%)	0 / 79 (0.00%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
erysipelas			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 394 (0.00%)	0 / 79 (0.00%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 394 (0.25%)	0 / 79 (0.00%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
sinusitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 394 (0.25%)	0 / 79 (0.00%)	0 / 79 (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 / 394 (0.00%)	0 / 79 (0.00%)	1 / 79 (1.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	IXE80Q2W Non-randomized Population to Withdrawal Period	IXE80Q2W Relapse Period	IXE80Q2W Post-Treatment Follow-up Period
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 133 (4.51%)	1 / 97 (1.03%)	4 / 355 (1.13%)
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)			
uterine leiomyoma			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed ^[1]	0 / 78 (0.00%)	0 / 53 (0.00%)	0 / 195 (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
General disorders and administration site conditions			
drowning			
alternative dictionary used:			

MedDRA 21.1			
subjects affected / exposed	0 / 133 (0.00%)	0 / 97 (0.00%)	0 / 355 (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
non-cardiac chest pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 133 (0.00%)	0 / 97 (0.00%)	0 / 355 (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			
endometriosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed ^[2]	0 / 78 (0.00%)	0 / 53 (0.00%)	0 / 195 (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
ovarian cyst			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed ^[3]	1 / 78 (1.28%)	0 / 53 (0.00%)	0 / 195 (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
Respiratory, thoracic and mediastinal disorders			
acute respiratory failure			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 133 (0.00%)	0 / 97 (0.00%)	1 / 355 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
respiratory failure			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 133 (0.00%)	0 / 97 (0.00%)	0 / 355 (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			
troponin increased			

alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 133 (0.00%)	0 / 97 (0.00%)	1 / 355 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
fall			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 133 (0.75%)	0 / 97 (0.00%)	0 / 355 (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
foreign body in eye			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 133 (0.00%)	0 / 97 (0.00%)	0 / 355 (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
humerus fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 133 (0.75%)	0 / 97 (0.00%)	0 / 355 (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
meniscus injury			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 133 (0.75%)	0 / 97 (0.00%)	0 / 355 (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
radius fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 133 (0.75%)	0 / 97 (0.00%)	0 / 355 (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
road traffic accident			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	1 / 133 (0.75%)	0 / 97 (0.00%)	0 / 355 (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
thermal burn			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 133 (0.00%)	0 / 97 (0.00%)	0 / 355 (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
upper limb fracture			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 133 (0.00%)	1 / 97 (1.03%)	0 / 355 (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
Cardiac disorders			
acute myocardial infarction			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 133 (0.00%)	0 / 97 (0.00%)	0 / 355 (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
angina unstable			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 133 (0.00%)	0 / 97 (0.00%)	0 / 355 (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
coronary artery disease			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 133 (0.00%)	0 / 97 (0.00%)	0 / 355 (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			
embolic stroke			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 133 (0.00%)	0 / 97 (0.00%)	0 / 355 (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
transient ischaemic attack			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 133 (0.00%)	0 / 97 (0.00%)	0 / 355 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
vascular headache			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 133 (0.00%)	0 / 97 (0.00%)	0 / 355 (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 / 133 (0.00%)	0 / 97 (0.00%)	0 / 355 (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
gastritis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 133 (0.00%)	0 / 97 (0.00%)	0 / 355 (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 necrosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 133 (0.00%)	0 / 97 (0.00%)	0 / 355 (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
intestinal obstruction			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 133 (0.00%)	0 / 97 (0.00%)	0 / 355 (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
large intestine polyp			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 133 (0.00%)	0 / 97 (0.00%)	0 / 355 (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
Hepatobiliary disorders			
cholecystitis acute			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 133 (0.00%)	0 / 97 (0.00%)	1 / 355 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cholelithiasis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 133 (0.75%)	0 / 97 (0.00%)	0 / 355 (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
hepatic steatosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 133 (0.00%)	0 / 97 (0.00%)	1 / 355 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
angioedema			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 133 (0.00%)	0 / 97 (0.00%)	0 / 355 (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			
foot deformity			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 133 (0.00%)	0 / 97 (0.00%)	0 / 355 (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 / 133 (0.00%)	0 / 97 (0.00%)	0 / 355 (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			
bronchitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	1 / 133 (0.75%)	0 / 97 (0.00%)	0 / 355 (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
erysipelas			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 133 (0.00%)	0 / 97 (0.00%)	1 / 355 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 133 (0.00%)	0 / 97 (0.00%)	0 / 355 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
sinusitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 133 (0.00%)	0 / 97 (0.00%)	0 / 355 (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 / 133 (0.00%)	0 / 97 (0.00%)	0 / 355 (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	Placebo Post-Treatment Follow-up Period		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
uterine leiomyoma			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed ^[1]	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
drowning			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
non-cardiac chest pain			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
endometriosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed ^[2]	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ovarian cyst			

alternative dictionary used: MedDRA 21.1			
subjects affected / exposed ^[3]	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
acute respiratory failure			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
respiratory failure			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
troponin increased			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
fall			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
foreign body in eye			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
humerus fracture			

alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
meniscus injury				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
radius fracture				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
road traffic accident				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
thermal burn				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
upper limb fracture				
alternative dictionary used: MedDRA 21.1				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
acute myocardial infarction				
alternative dictionary used: MedDRA 21.1				

subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
angina unstable			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
coronary artery disease			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
embolic stroke			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
transient ischaemic attack			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
vascular headache			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
crohn's disease			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
gastritis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
gastrointestinal necrosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
intestinal obstruction			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
large intestine polyp			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
cholecystitis acute			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
cholelithiasis			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
hepatic steatosis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
angioedema			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
foot deformity			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
osteoarthritis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
bronchitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
erysipelas			
alternative dictionary used: MedDRA 21.1			

subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
pneumonia			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
sinusitis			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
urinary tract infection			
alternative dictionary used: MedDRA 21.1			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	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: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

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

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

[3] - 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: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

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

Non-serious adverse events	Ixekizumab Open Label	Ixekizumab	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	143 / 394 (36.29%)	25 / 79 (31.65%)	14 / 79 (17.72%)
Investigations			
alanine aminotransferase increased			
alternative dictionary used: MedDRA 21.1			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>11 / 394 (2.79%)</p> <p>14</p>	<p>4 / 79 (5.06%)</p> <p>4</p>	<p>1 / 79 (1.27%)</p> <p>2</p>
<p>aspartate aminotransferase increased</p> <p>alternative dictionary used: MedDRA 21.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>6 / 394 (1.52%)</p> <p>8</p>	<p>4 / 79 (5.06%)</p> <p>4</p>	<p>1 / 79 (1.27%)</p> <p>2</p>
<p>Neoplasms benign, malignant and unspecified (incl cysts and polyps)</p> <p>uterine leiomyoma</p> <p>alternative dictionary used: MedDRA 21.1</p> <p>subjects affected / exposed^[4]</p> <p>occurrences (all)</p> <p>0 / 212 (0.00%)</p> <p>0</p>	<p>2 / 32 (6.25%)</p> <p>2</p>	<p>0 / 39 (0.00%)</p> <p>0</p>
<p>General disorders and administration site conditions</p> <p>injection site reaction</p> <p>alternative dictionary used: MedDRA 21.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>59 / 394 (14.97%)</p> <p>270</p>	<p>1 / 79 (1.27%)</p> <p>8</p>	<p>0 / 79 (0.00%)</p> <p>0</p>
<p>Skin and subcutaneous tissue disorders</p> <p>psoriasis</p> <p>alternative dictionary used: MedDRA 21.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>2 / 394 (0.51%)</p> <p>2</p>	<p>0 / 79 (0.00%)</p> <p>0</p>	<p>4 / 79 (5.06%)</p> <p>4</p>
<p>Infections and infestations</p> <p>bronchitis</p> <p>alternative dictionary used: MedDRA 21.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>18 / 394 (4.57%)</p> <p>23</p> <p>nasopharyngitis</p> <p>alternative dictionary used: MedDRA 21.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>34 / 394 (8.63%)</p> <p>37</p> <p>oral herpes</p> <p>alternative dictionary used: MedDRA 21.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>9 / 394 (2.28%)</p> <p>10</p>	<p>4 / 79 (5.06%)</p> <p>4</p> <p>11 / 79 (13.92%)</p> <p>13</p> <p>4 / 79 (5.06%)</p> <p>9</p>	<p>1 / 79 (1.27%)</p> <p>1</p> <p>4 / 79 (5.06%)</p> <p>4</p> <p>1 / 79 (1.27%)</p> <p>3</p>

upper respiratory tract infection alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	49 / 394 (12.44%) 66	9 / 79 (11.39%) 14	4 / 79 (5.06%) 5
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Non-serious adverse events	IXE80Q2W Non-randomized Population to Withdrawal Period	IXE80Q2W Relapse Period	IXE80Q2W Post-Treatment Follow-up Period
Total subjects affected by non-serious adverse events subjects affected / exposed	37 / 133 (27.82%)	30 / 97 (30.93%)	19 / 355 (5.35%)
Investigations alanine aminotransferase increased alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	2 / 133 (1.50%) 2	1 / 97 (1.03%) 2	3 / 355 (0.85%) 3
aspartate aminotransferase increased alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	1 / 133 (0.75%) 1	1 / 97 (1.03%) 3	2 / 355 (0.56%) 2
Neoplasms benign, malignant and unspecified (incl cysts and polyps) uterine leiomyoma alternative dictionary used: MedDRA 21.1 subjects affected / exposed ^[4] occurrences (all)	0 / 78 (0.00%) 0	0 / 53 (0.00%) 0	0 / 195 (0.00%) 0
General disorders and administration site conditions injection site reaction alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	2 / 133 (1.50%) 20	7 / 97 (7.22%) 27	0 / 355 (0.00%) 0
Skin and subcutaneous tissue disorders psoriasis alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	2 / 133 (1.50%) 3	1 / 97 (1.03%) 1	4 / 355 (1.13%) 4
Infections and infestations			

bronchitis alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	5 / 133 (3.76%) 5	4 / 97 (4.12%) 5	0 / 355 (0.00%) 0
nasopharyngitis alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	19 / 133 (14.29%) 22	13 / 97 (13.40%) 17	2 / 355 (0.56%) 2
oral herpes alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	2 / 133 (1.50%) 3	2 / 97 (2.06%) 2	2 / 355 (0.56%) 2
upper respiratory tract infection alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	12 / 133 (9.02%) 18	9 / 97 (9.28%) 10	8 / 355 (2.25%) 8

Non-serious adverse events	Placebo Post-Treatment Follow-up Period		
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 12 (0.00%)		
Investigations alanine aminotransferase increased alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all) aspartate aminotransferase increased alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0 0 / 12 (0.00%) 0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps) uterine leiomyoma alternative dictionary used: MedDRA 21.1 subjects affected / exposed ^[4] occurrences (all)	0 / 6 (0.00%) 0		

General disorders and administration site conditions injection site reaction alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Skin and subcutaneous tissue disorders psoriasis alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Infections and infestations bronchitis alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all) nasopharyngitis alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all) oral herpes alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all) upper respiratory tract infection alternative dictionary used: MedDRA 21.1 subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0		

Notes:

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

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported