Clinical trial results:
A 24-Week Multicenter, Randomized, Open-Label, Parallel-Group Study Comparing the Efficacy and Safety of Ixekizumab to Fumaric Acid Esters and Methotrexate in Patients With Moderate-to-Severe Plaque Psoriasis Who Are Naive to Systemic Treatment With an Extension Period

Summary

EudraCT number	2015-002649-69
Trial protocol	DE
Global end of trial date	14 November 2017

Results information

Result version number	v1 (current)
This version publication date	28 November 2018
First version publication date	28 November 2018

Trial information

Trial identification

Sponsor protocol code	I1F-EW-RHBZ

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02634801
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 16190

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	14 November 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 November 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study is to evaluate the efficacy and safety of ixekizumab compared to fumaric acid esters (FAE) and methotrexate (MTX) in participants with moderate-to-severe plaque psoriasis who are naive to systemic treatment.

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	20 January 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 162
Worldwide total number of subjects	162
EEA total number of subjects	162

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)	154
From 65 to 84 years	8

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Treatment Period (Weeks 0 to 24), Extension Period (Weeks 24 to 36) followed by post-treatment follow-up period occurring from last treatment visit (week 36), or Early Termination Visit (ETV) up to a minimum of 12 weeks following that visit.

Pre-assignment

Screening details:

Not applicable

Period 1

Period 1 title	Treatment Period (Weeks 0 to 24)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Ixekizumab

Arm description:

160 milligrams (mg) ixekizumab given as two subcutaneous injections (SC) followed by 80 mg ixekizumab given SC every 2 weeks until week 12 and then 80 mg ixekizumab given SC every 4 weeks until week 24. Extension Period: At week 24, participants have the option to continue ixekizumab treatment for up to 36 weeks.

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

Dosage and administration details:

160 mg ixekizumab given as two subcutaneous (SC)injection followed by 80 mg ixekizumab given SC every 2 weeks until week 12 and then 80 mg ixekizumab given SC every 4 weeks until week 24. In extension period at week 24, participants have the option to continue ixekizumab treatment for up to 36 weeks.

Arm title	Fumaric Acid Esters

Arm description:

Starting dose of 105 mg Fumaric Acid Esters (FAE) given orally followed by 215 mg FAE given orally 1 to 3 times per day until week 24. Extension Period: At week 24, participants have the option to begin ixekizumab treatment for up to 36 weeks.

Arm type	Active comparator
Investigational medicinal product name	Fumaric Acid Esters
Investigational medicinal product code	
Other name	Fumaderm initial; FAE
Pharmaceutical forms	Gastro-resistant tablet
Routes of administration	Oral use

Dosage and administration details:

FAE was administered as oral tablets. After starting oral FAE 105 mg (Fumaderm initial; until exhaustion of the package), FAE 215 mg (Fumaderm) was given orally immediately thereafter.

Arm title	Methotrexate

Arm description:

7.5 mg starting dose up to 30 mg Methotrexate (MTX) given orally once a week until week 24. Extension Period: At week 24, participants have the option to begin ixekizumab treatment for up to 36 weeks.

Arm type	Active comparator
Investigational medicinal product name	Methotrexate
Investigational medicinal product code	
Other name	Lantarel
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

MTX was administered as oral tablets, starting with 7.5 mg/week, with a stepwise increase in dosage of 5 mg to 7.5 mg/week until a dose of 15 mg/week was reached.

Number of subjects in period 1	Ixekizumab	Fumaric Acid Esters	Methotrexate
Started	54	54	54
Received at Least 1 Dose of Study Drug	54	52	52
Completed	50	23	49
Not completed	4	31	5
Consent withdrawn by subject	-	8	3
Adverse event, non-fatal	2	20	-
Lost to follow-up	2	1	1
Lack of efficacy	-	2	-
Protocol deviation	-	-	1

Period 2

Period 2 title	Extension Period (Weeks 24 to 36)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Ixekizumab

Arm description:

160 milligrams (mg) ixekizumab given as two subcutaneous injections (SC) followed by 80 mg ixekizumab given SC every 2 weeks until week 12 and then 80 mg ixekizumab given SC every 4 weeks until week 24. Extension Period: At week 24, participants have the option to continue ixekizumab treatment for up to 36 weeks.

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

Dosage and administration details:

160 mg ixekizumab given as two subcutaneous (SC)injection followed by 80 mg ixekizumab given SC every 2 weeks until week 12 and then 80 mg ixekizumab given SC every 4 weeks until week 24. In

extension period at week 24, participants have the option to continue ixekizumab treatment for up to 36 weeks.

Arm title	Fumaric Acid Esters

Arm description:

Starting dose of 105 mg Fumaric Acid Esters (FAE) given orally followed by 215 mg FAE given orally 1 to 3 times per day until week 24. Extension Period: At week 24, participants have the option to begin ixekizumab treatment for up to 36 weeks.

Arm type	Active comparator
Investigational medicinal product name	Fumaric Acid Esters
Investigational medicinal product code	
Other name	Fumaderm initial; FAE
Pharmaceutical forms	Gastro-resistant tablet
Routes of administration	Oral use

Dosage and administration details:

FAE was administered as oral tablets. After starting oral FAE 105 mg (Fumaderm initial; until exhaustion of the package), FAE 215 mg (Fumaderm) was given orally immediately thereafter.

Arm title	Methotrexate

Arm description:

7.5 mg starting dose up to 30 mg Methotrexate (MTX) given orally once a week until week 24. Extension Period: At week 24, participants have the option to begin ixekizumab treatment for up to 36 weeks.

Arm type	Active comparator
Investigational medicinal product name	Methotrexate
Investigational medicinal product code	
Other name	Lantarel
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

MTX was administered as oral tablets, starting with 7.5 mg/week, with a stepwise increase in dosage of 5 mg to 7.5 mg/week until a dose of 15 mg/week was reached.

Number of subjects in period 2[1]	Ixekizumab	Fumaric Acid Esters	Methotrexate
Started	48	19	31
Completed	45	18	29
Not completed	3	1	2
Consent withdrawn by subject	1	1	1
Adverse event, non-fatal	-	-	1
Lost to follow-up	1	-	-
Missing	1	-	-

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: Participants who discontinued previous periods had option to enter post treatment followup period.

Period 3

Period 3 title	Followup
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Ixekizumab

Arm description:

160 milligrams (mg) ixekizumab given as two subcutaneous injections (SC) followed by 80 mg ixekizumab given SC every 2 weeks until week 12 and then 80 mg ixekizumab given SC every 4 weeks until week 24. Extension Period: At week 24, participants have the option to continue ixekizumab treatment for up to 36 weeks.

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

Dosage and administration details:

160 mg ixekizumab given as two subcutaneous (SC)injection followed by 80 mg ixekizumab given SC every 2 weeks until week 12 and then 80 mg ixekizumab given SC every 4 weeks until week 24. In extension period at week 24, participants have the option to continue ixekizumab treatment for up to 36 weeks.

Arm title	Fumaric Acid Esters

Arm description:

Starting dose of 105 mg Fumaric Acid Esters (FAE) given orally followed by 215 mg FAE given orally 1 to 3 times per day until week 24. Extension Period: At week 24, participants have the option to begin ixekizumab treatment for up to 36 weeks.

Arm type	Active comparator
Investigational medicinal product name	Fumaric Acid Esters
Investigational medicinal product code	
Other name	Fumaderm initial; FAE
Pharmaceutical forms	Gastro-resistant tablet
Routes of administration	Oral use

Dosage and administration details:

FAE was administered as oral tablets. After starting oral FAE 105 mg (Fumaderm initial; until exhaustion of the package), FAE 215 mg (Fumaderm) was given orally immediately thereafter.

Arm title	Methotrexate

Arm description:

7.5 mg starting dose up to 30 mg Methotrexate (MTX) given orally once a week until week 24. Extension Period: At week 24, participants have the option to begin ixekizumab treatment for up to 36 weeks.

Arm type	Active comparator
Investigational medicinal product name	Methotrexate
Investigational medicinal product code	
Other name	Lantarel
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

MTX was administered as oral tablets, starting with 7.5 mg/week, with a stepwise increase in dosage of 5 mg to 7.5 mg/week until a dose of 15 mg/week was reached.

Number of subjects in period 3	Ixekizumab	Fumaric Acid Esters	Methotrexate
Started	41	26	46
Completed	36	18	38
Not completed	5	8	8
Consent withdrawn by subject	1	2	5
Physician decision	-	-	1
Adverse event, non-fatal	1	5	-
Lost to follow-up	3	1	2

Baseline characteristics

Reporting groups	
Reporting group title	Ixekizumab
Reporting group description:	
160 milligrams (mg) ixekizumab given as two subcutaneous injections (SC) followed by 80 mg ixekizumab given SC every 2 weeks until week 12 and then 80 mg ixekizumab given SC every 4 weeks until week 24. Extension Period: At week 24, participants have the option to continue ixekizumab treatment for up to 36 weeks.	
Reporting group title	Fumaric Acid Esters
Reporting group description:	
Starting dose of 105 mg Fumaric Acid Esters (FAE) given orally followed by 215 mg FAE given orally 1 to 3 times per day until week 24. Extension Period: At week 24, participants have the option to begin ixekizumab treatment for up to 36 weeks.	
Reporting group title	Methotrexate
Reporting group description:	
7.5 mg starting dose up to 30 mg Methotrexate (MTX) given orally once a week until week 24. Extension Period: At week 24, participants have the option to begin ixekizumab treatment for up to 36 weeks.	

Reporting group values	Ixekizumab	Fumaric Acid Esters	Methotrexate
Number of subjects	54	54	54
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	44.3	43.1	38.7
standard deviation	± 13.84	± 14.16	± 12.90
Sex: Female, Male Units: Subjects			
Female	12	11	18
Male	42	43	36
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	0	3
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	43	44	42
More than one race	10	10	9
Unknown or Not Reported	0	0	0

Region of Enrollment Units: Subjects			
Germany	54	54	54

Reporting group values	Total		
Number of subjects	162		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Subjects			
Female	41		
Male	121		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	4		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	129		
More than one race	29		
Unknown or Not Reported	0		
Region of Enrollment Units: Subjects			
Germany	162		

End points

End points reporting groups

Reporting group title	Ixekizumab

Reporting group description:

160 milligrams (mg) ixekizumab given as two subcutaneous injections (SC) followed by 80 mg ixekizumab given SC every 2 weeks until week 12 and then 80 mg ixekizumab given SC every 4 weeks until week 24. Extension Period: At week 24, participants have the option to continue ixekizumab treatment for up to 36 weeks.

Reporting group title	Fumaric Acid Esters

Reporting group description:

Starting dose of 105 mg Fumaric Acid Esters (FAE) given orally followed by 215 mg FAE given orally 1 to 3 times per day until week 24. Extension Period: At week 24, participants have the option to begin ixekizumab treatment for up to 36 weeks.

Reporting group title	Methotrexate

Reporting group description:

7.5 mg starting dose up to 30 mg Methotrexate (MTX) given orally once a week until week 24. Extension Period: At week 24, participants have the option to begin ixekizumab treatment for up to 36 weeks.

Reporting group title	Ixekizumab

Reporting group description:

160 milligrams (mg) ixekizumab given as two subcutaneous injections (SC) followed by 80 mg ixekizumab given SC every 2 weeks until week 12 and then 80 mg ixekizumab given SC every 4 weeks until week 24. Extension Period: At week 24, participants have the option to continue ixekizumab treatment for up to 36 weeks.

Reporting group title	Fumaric Acid Esters

Reporting group description:

Starting dose of 105 mg Fumaric Acid Esters (FAE) given orally followed by 215 mg FAE given orally 1 to 3 times per day until week 24. Extension Period: At week 24, participants have the option to begin ixekizumab treatment for up to 36 weeks.

Reporting group title	Methotrexate

Reporting group description:

7.5 mg starting dose up to 30 mg Methotrexate (MTX) given orally once a week until week 24. Extension Period: At week 24, participants have the option to begin ixekizumab treatment for up to 36 weeks.

Reporting group title	Ixekizumab

Reporting group description:

160 milligrams (mg) ixekizumab given as two subcutaneous injections (SC) followed by 80 mg ixekizumab given SC every 2 weeks until week 12 and then 80 mg ixekizumab given SC every 4 weeks until week 24. Extension Period: At week 24, participants have the option to continue ixekizumab treatment for up to 36 weeks.

Reporting group title	Fumaric Acid Esters

Reporting group description:

Starting dose of 105 mg Fumaric Acid Esters (FAE) given orally followed by 215 mg FAE given orally 1 to 3 times per day until week 24. Extension Period: At week 24, participants have the option to begin ixekizumab treatment for up to 36 weeks.

Reporting group title	Methotrexate

Reporting group description:

7.5 mg starting dose up to 30 mg Methotrexate (MTX) given orally once a week until week 24. Extension Period: At week 24, participants have the option to begin ixekizumab treatment for up to 36 weeks.

Primary: Percentage of Participants with a ≥75% Improvement in Psoriasis Area and Severity Index (PASI 75) at Week 24

End point title	Percentage of Participants with a ≥75% Improvement in Psoriasis Area and Severity Index (PASI 75) at Week 24

End point description:

The PASI combines the extent of body surface involvement in 4 anatomical regions (head, trunk, arms, and legs). For each region the percent area of skin involved was estimated from 0 (0%) to 6 (90%-100%) and severity was estimated by clinical signs of erythema, induration and scaling with a scores range from 0 (no involvement) to 4 (severe involvement). Each area is scored separately and the scores then combined for the final PASI. Final PASI calculated as: sum of severity parameters for each region * area score * weighing factor [head (0.1), upper limbs (0.2), trunk (0.3), lower limbs (0.4)]. Overall scores range from 0 (no Ps) to 72 (the most severe disease).
Analysis Population Description (APD): All randomized participants who had a post-baseline measurement for PASI 75. Participants who did not meet the clinical response criteria or had missing data were considered non-responders for Non-Responder Imputation (NRI) analysis.

End point type	Primary

End point timeframe:

Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	54	54	
Units: Percentage of Participants				
number (not applicable)	90.7	22.2	70.4	

Statistical analyses

Statistical analysis title	PASI 75
Comparison groups	Fumaric Acid Esters v Ixekizumab
Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Fisher exact
Parameter estimate	Risk ratio (RR)
Point estimate	4.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.46
upper limit	6.77

Statistical analysis title	PASI 75
Comparison groups	Ixekizumab v Methotrexate

Number of subjects included in analysis	108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0137
Method	Fisher exact
Parameter estimate	Risk ratio (RR)
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	1.56

Secondary: Percentage of Participants with a ≥90% Improvement in Psoriasis Area and Severity Index (PASI 90) from Baseline

End point title	Percentage of Participants with a ≥90% Improvement in Psoriasis Area and Severity Index (PASI 90) from Baseline

End point description:

The PASI combines the extent of body surface involvement in 4 anatomical regions (head, trunk, arms, and legs). For each region the percent area of skin involved was estimated from 0 (0%) to 6 (90%-100%) and severity was estimated by clinical signs of erythema, induration and scaling with a scores range from 0 (no involvement) to 4 (severe involvement). Each area is scored separately and the scores then combined for the final PASI. Final PASI calculated as: sum of severity parameters for each region * area score * weighing factor [head (0.1), upper limbs (0.2), trunk (0.3), lower limbs (0.4)]. Overall scores range from 0 (no Ps) to 72 (the most severe disease).
APD: All randomized participants who had a post-baseline measurement for PASI 90. Participants who did not meet the clinical response criteria or had missing data were considered non-responders for Non-Responder Imputation (NRI) analysis.

End point type	Secondary

End point timeframe:

Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	54	54	
Units: Percentage of Participants				
number (not applicable)	79.6	9.3	38.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a 100% Improvement in Psoriasis Area and Severity Index (PASI 100) from Baseline

End point title	Percentage of Participants with a 100% Improvement in Psoriasis Area and Severity Index (PASI 100) from Baseline

End point description:

The PASI combines the extent of body surface involvement in 4 anatomical regions (head, trunk, arms, and legs). For each region the percent area of skin involved was estimated from 0 (0%) to 6 (90%-100%) and severity was estimated by clinical signs of erythema, induration and scaling with a scores range from 0 (no involvement) to 4 (severe involvement). Each area is scored separately and the scores then combined for the final PASI. Final PASI calculated as: sum of severity parameters for each region * area score * weighing factor [head (0.1), upper limbs (0.2), trunk (0.3), lower limbs (0.4)]. Overall scores range from 0 (no Ps) to 72 (the most severe disease).
APD: All randomized participants who had a post-baseline measurement for PASI 100. Participants who did not meet the clinical response criteria or had missing data were considered non-responders for Non-Responder Imputation (NRI) analysis.

End point type	Secondary

End point timeframe:

Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	54	54	
Units: Percentage of Participants				
number (not applicable)	40.7	3.7	13.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in PASI Total Score

End point title	Change from baseline in PASI Total Score

End point description:

The PASI combines the extent of body surface involvement in 4 anatomical regions (head, trunk, arms, and legs). For each region the percent area of skin involved was estimated from 0 (0%) to 6 (90%-100%) and severity was estimated by clinical signs of erythema, induration and scaling with a scores range from 0 (no involvement) to 4 (severe involvement). Each area is scored separately and the scores then combined for the final PASI. Final PASI calculated as: sum of severity parameters for each region * area score * weighing factor [head (0.1), upper limbs (0.2), trunk (0.3), lower limbs (0.4)]. Overall scores range from 0 (no Ps) to 72 (the most severe disease). LS mean change from baseline in PASI was calculated using Analysis of Covariance (ANCOVA) with modified Baseline- Observation- Carried Forward (mBOCF) and with terms for baseline and treatment.
APD: All randomized participants who received at least 1 dose of study drug and had baseline and a post-baseline measurement for PASI.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	50	52	
Units: units on a scale				
least squares mean (confidence interval 95%)	-16.68 (-18.46 to -14.91)	-4.93 (-6.78 to -3.09)	-14.61 (-16.42 to -12.80)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a Static Physician Global Assessment (sPGA) (0,1) and ≥2 Point Improvement from Baseline among those with sPGA Score ≥3 at Baseline

End point title	Percentage of Participants with a Static Physician Global Assessment (sPGA) (0,1) and ≥2 Point Improvement from Baseline among those with sPGA Score ≥3 at Baseline

End point description:

The sPGA is the physician's determination of the participant's Psoriasis (Ps) lesions overall at a given time point. Lesions were categorized by descriptions for induration, erythema, and scaling. Participants Ps were assessed as 0 (clear), 1 (minimal), 2 (mild), 3 (moderate), 4 (severe), or 5 (very severe). An sPGA responder was defined as having a post-baseline sPGA score of "0" or "1" with at least a 2-point improvement from baseline.
APD: All randomized participants with baseline sPGA >=3 & received at least 1 dose of study drug and had a post-baseline measurement for sPGA. Participants who did not meet the clinical response criteria or had missing data were considered non-responders for Non-Responder Imputation (NRI) analysis.

End point type	Secondary

End point timeframe:

Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	53	52	
Units: Percentage of Participants				
number (not applicable)	86.5	13.2	51.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving DLQI (0,1)

End point title	Percentage of Participants Achieving DLQI (0,1)

End point description:

The DLQI is a simple, participant-administered, 10 question, validated, quality-of-life questionnaire that covers 6 domains: symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment. Response categories include "not at all," "a lot," and "very much," with

corresponding scores of 1, 2, and 3, respectively, and unanswered ("not relevant") responses scored as "0." Totals range from 0 to 30 (less to more impairment), and a 5-point change from baseline is considered clinically relevant.
APD: All randomized participants who had a post-baseline measurement for DLQI. Participants who did not meet the clinical response criteria or had missing data were considered non-responders for Non-Responder Imputation (NRI) analysis.

End point type	Secondary

End point timeframe:

Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	54	54	
Units: Percentage of Participants				
number (not applicable)	63.0	14.8	37.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline on Dermatology Life Quality Index (DLQI) Total Score

End point title	Change from Baseline on Dermatology Life Quality Index (DLQI) Total Score

End point description:

The DLQI is a simple, participant-administered, 10 question, validated, quality-of-life questionnaire that covers 6 domains: symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment. Response categories include "not at all," "a lot," and "very much," with corresponding scores of 1, 2, and 3, respectively, and unanswered ("not relevant") responses scored as "0." Totals range from 0 to 30 (less to more impairment), and a 5-point change from baseline is considered clinically relevant. LS mean change from baseline in DLQI was calculated using ANCOVA with mBOCF and with terms for baseline and treatment.
APD: All randomized participants who received at least 1 dose of study drug and had baseline and a post-baseline measurement for DLQI.
mBOCF: Participants who discontinued treatment due to AE were imputed by their baseline observation, Participants who discontinued due to other reasons were imputed by their last observation.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	49	49	
Units: units on a scale				
least squares mean (confidence interval 95%)	-13.08 (-14.56 to -11.61)	-5.37 (-6.88 to -3.86)	-12.81 (-14.32 to -11.29)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Body Surface Area (BSA) Affected by Psoriasis

End point title	Change from Baseline in Body Surface Area (BSA) Affected by Psoriasis

End point description:

The percentage involvement of psoriasis on each participant's body surface area was assessed by the investigator on a continuous scale from 0% (no involvement) to 100% (full involvement), in which 1% corresponds to the size of the participant's hand including palm, fingers and thumb. LS mean change from baseline in BSA was calculated using ANCOVA with mBOCF and with terms for baseline and treatment.
APD: All randomized participants who received at least 1 dose of study drug and had baseline and a post-baseline measurement for BSA.
mBOCF: Participants who discontinued treatment due to AE were imputed by their baseline observation, Participants who discontinued due to other reasons were imputed by their last observation.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	50	52	
Units: % Body Surface Affected				
least squares mean (confidence interval 95%)	-20.64 (-23.21 to -18.08)	-5.26 (-7.93 to -2.60)	-18.46 (-21.08 to -15.85)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Palmoplantar Psoriasis Severity Index (PPASI) Total Score

End point title	Change from Baseline in Palmoplantar Psoriasis Severity Index (PPASI) Total Score

End point description:

The Palmoplantar PASI is a composite score derived from the sum scores for erythema, induration, and desquamation multiplied by a score for the extent of palm and sole area involvement, ranging from 0 (no PPASI) to 72 (most severe PPASI). The PPASI was only assessed if participants have palmoplantar psoriasis at baseline. LS mean change from baseline in PPASI was calculated using ANCOVA with mBOCF and with terms for baseline and treatment.
APD: All randomized participants who received at least 1 dose of study drug and had baseline and a post-baseline measurement for PPASI.

mBOCF: Participants who discontinued treatment due to AE were imputed by their baseline observation, Participants who discontinued due to other reasons were imputed by their last observation.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	14	9	
Units: units on a scale				
least squares mean (confidence interval 95%)	-7.23 (-10.88 to -3.59)	-2.45 (-6.03 to 1.13)	-3.77 (-8.10 to 0.56)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Psoriasis Scalp Severity Index (PSSI) Total Score

End point title	Change from Baseline in Psoriasis Scalp Severity Index (PSSI) Total Score

End point description:

The PSSI is a physician assessment of erythema, induration and desquamation and percent of scalp that is covered with a scores range from 0 (none) to 4 (very severe). The composite score is derived from the sum of scores for erythema, induration, and desquamation multiplied by the score recorded for the extent of the scalp area involved, 1 (<10%) to 6 (90%-100%) with a total score ranging from 0 (less severity) to 72 (more severity). LS mean change from baseline in PSSI was calculated using ANCOVA with mBOCF and with terms for baseline and treatment.
APD: All randomized participants who received at least 1 dose of study drug and had baseline and a post-baseline measurement for Psoriasis Scalp.
mBOCF: Participants who discontinued treatment due to AE were imputed by their baseline observation, Participants who discontinued due to other reasons were imputed by their last observation.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	39	40	
Units: units on a scale				
least squares mean (confidence interval 95%)	-20.85 (-23.63 to -18.06)	-6.76 (-9.58 to -3.94)	-18.56 (-21.35 to -15.78)	

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Benefit Index (PBI) overall benefit score

End point title	Patient Benefit Index (PBI) overall benefit score

End point description:

The PBI assessment consists of 2 steps: before treatment, every patient defines his/her treatment needs according to a standardized list (Patient Needs Questionnaire [PNQ]). After treatment, the patient rates the degree of benefits achieved (Patient Benefits Questionnaire [PBQ]). 25 items are rated on a 5-point scale with values from 0 (not at all) to 4 (very), allowing for "did not apply to me" (5) and missing. For each treatment goal the PNQ importance is derived by dividing the respective PNQ item by the sum of all PNQ items. The weighted sum of each PBQ item with its respective PNQ importance yields the PBI score. LS mean was calculated using ANCOVA with LOCF and with a term for treatment.
APD: All randomized participants who received at least 1 dose of study drug and had a baseline PBI questionnaire such that postbaseline PBI assessments can be valid (nonmissing).

End point type	Secondary

End point timeframe:

Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	43	41	50	
Units: units on a scale				
least squares mean (confidence interval 95%)	3.42 (2.99 to 3.84)	2.33 (1.81 to 2.84)	2.66 (2.23 to 3.10)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline on Itch Numeric Rating Scale (NRS) Score

End point title	Change from Baseline on Itch Numeric Rating Scale (NRS) Score

End point description:

The Itch NRS is a participant-administered single-item 11-point horizontal scale anchored at 0 and 10, with 0 representing "no itch" and 10 representing "worst itch imaginable." Overall severity of a participant's itching from psoriasis (Ps) is indicated by circling the number that best describes the worst level of itching in the past 24 hours. LS mean change from baseline was calculated using ANCOVA with mBOCF and with terms for baseline and treatment.
APD: All randomized participants who received at least 1 dose of study drug and had baseline and a post-baseline measurement for Itch NRS score.
mBOCF: Participants who discontinued treatment due to AE were imputed by their baseline observation, Participants who discontinued due to other reasons were imputed by their last observation.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	50	52	
Units: units on a scale				
least squares mean (confidence interval 95%)	-5.25 (-5.89 to -4.61)	-1.50 (-2.15 to -0.84)	-4.40 (-5.05 to -3.76)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline on the Skin Pain Visual Analog Scale (VAS)

End point title	Change from Baseline on the Skin Pain Visual Analog Scale (VAS)

End point description:

The pain VAS is a participant-administered single-item scale designed to measure Skin pain from Psoriasis using a 100 millimeter (mm) horizontal VAS. Overall severity of participant's skin pain from Psoriasis is indicated by placing a single mark on the horizontal 100 mm scale from 0 mm (no pain) to 100 mm (pain as severe as you can imagine). LS mean change from baseline was calculated using ANCOVA with mBOCF and with terms for baseline and treatment.
APD: All randomized participants who received at least 1 dose of study drug and had baseline and a post-baseline measurement for skin pain VAS.
mBOCF: Participants who discontinued treatment due to AE were imputed by their baseline observation, Participants who discontinued due to other reasons were imputed by their last observation.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	50	52	
Units: Millimeter (mm)				
least squares mean (confidence interval 95%)	-33.83 (-39.46 to -28.20)	-7.20 (-12.99 to -1.42)	-28.29 (-33.98 to -22.60)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline on Quick Inventory of Depressive Symptomatology-Self Report (16 items) (QIDS-SR16)

End point title	Change from Baseline on Quick Inventory of Depressive Symptomatology-Self Report (16 items) (QIDS-SR16)

End point description:

QIDS-SR16 is a participant-administered, 16-item instrument intended to assess the existence and severity of symptoms of depression. A participant is asked to consider each statement as it relates to the way they have felt for the past 7 days and rate each on a 4-point scale: 0 (best) to 3 (worst). The

sum of the 16 items corresponding to 9 depression domains [sad mood, concentration, self-criticism, suicidal ideation, interest, energy/fatigue, sleep disturbance (initial, middle and late insomnia or hypersomnia), decrease/increase in appetite/weight, and psychomotor agitation/retardation] to give a single total scores range from 0 to 27, with higher scores indicating greater symptom severity. Whereas 0-5 indicates no symptoms. LS mean change from baseline was calculated using ANCOVA with mBOCF and with terms for baseline and treatment.
APD: All randomized participants who received at least 1 dose of study drug and had baseline and a post-baseline measurement for QIDS-SR16.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	49	50	
Units: units on a scale				
least squares mean (confidence interval 95%)	-2.16 (-3.00 to -1.32)	-1.01 (-1.89 to -0.14)	-2.50 (-3.37 to -1.64)	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The SF-36 is a participant-reported outcome measure evaluating participant's health status. It comprises 36 items covering 8 domains: physical functioning, role physical, role emotional, bodily pain, vitality, social functioning, mental health, and general health. Items are answered on Likert scales of varying lengths. The 8 domains are regrouped into the PCS and MCS scores. The summary scores range from 0 to 100, lower scores = more disability, higher scores = less disability and better health. In this study, the SF-36 acute version was used, which has a 1-week recall period. LS mean change from baseline was calculated using ANCOVA with mBOCF and with terms for baseline and treatment.

APD: All randomized participants who received at least 1 dose of study drug and had baseline and a post-baseline measurement for SF36 PCS score.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	48	49	
Units: units on a scale				
least squares mean (confidence interval 95%)	4.45 (2.29 to 6.60)	0.57 (-1.64 to 2.77)	4.01 (1.83 to 6.19)	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The SF-36 is a participant-reported outcome measure evaluating participant's health status. It comprises 36 items covering 8 domains: physical functioning, role physical, role emotional, bodily pain, vitality, social functioning, mental health, and general health. Items are answered on Likert scales of varying lengths. The 8 domains are regrouped into the PCS and MCS scores. The summary scores range from 0 to 100, lower scores = more disability, higher scores = less disability and better health. In this study, the SF-36 acute version was used, which has a 1-week recall period. LS mean change from baseline was calculated using ANCOVA with mBOCF and with terms for baseline and treatment.

APD: All randomized participants who received at least 1 dose of study drug and had baseline and a post-baseline measurement for SF36 MCS score.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	48	49	
Units: units on a scale				
least squares mean (confidence interval 95%)	7.13 (4.99 to 9.27)	3.39 (1.19 to 5.59)	6.99 (4.80 to 9.17)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline on Patient’s Global Assessment (PatGA) of Disease Severity

End point title	Change from Baseline on Patient’s Global Assessment (PatGA) of Disease Severity

End point description:

The PatGA is a single-item self-reported instrument asking the participant to rate the severity of their

psoriasis "today" by circling a number on the numeric rating scale from 0 (Clear = no psoriasis) to 5 (Severe = the worst their psoriasis has ever been). LS mean change from baseline was calculated using ANCOVA with mBOCF and with terms for baseline and treatment.

APD: All randomized participants who received at least 1 dose of study drug and had baseline and a post-baseline measurement for PatGA.
mBOCF: Participants who discontinued treatment due to AE were imputed by their baseline observation, Participants who discontinued due to other reasons were imputed by their last observation.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	50	50	
Units: units on a scale				
least squares mean (confidence interval 95%)	-3.12 (-3.47 to -2.78)	-0.87 (-1.23 to -0.51)	-2.39 (-2.75 to -2.04)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline on the Psoriasis Skin Appearance Bothersomeness (PSAB) total score

End point title	Change from Baseline on the Psoriasis Skin Appearance Bothersomeness (PSAB) total score

End point description:

PSAB measure is a 3-item scale designed to measure the degree of bothersomeness of skin appearance due to Ps in participants with Ps. Participants are asked to indicate on 3 numeric rating scales (NRS) from 0 (not at all bothered) to 10 (extremely bothered) how bothered they are by any redness or discoloration, thickness, and scaling or flaking on their skin due to Ps. The scores from the 3 NRS items are summed for a total score ranging from 0 to 30, where 0 indicating no bothersomeness and 30 indicating greater bothersomeness. LS mean change from baseline was calculated using ANCOVA with mBOCF and with terms for baseline and treatment.

APD: All randomized participants who received at least 1 dose of study drug and had baseline and a post-baseline measurement for PSAB.
mBOCF: Participants who discontinued treatment due to AE were imputed by their baseline observation, Participants who discontinued due to other reasons were imputed by their last observation.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	47	48	
Units: units on a scale				
least squares mean (confidence interval 95%)	-19.87 (-22.38 to 17.36)	-5.18 (-7.82 to -2.54)	-15.05 (-17.67 to -12.43)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline on the Nail Assessment in Psoriasis and Psoriatic Arthritis (NAPPA-CLIN) Total Score

End point title	Change from Baseline on the Nail Assessment in Psoriasis and Psoriatic Arthritis (NAPPA-CLIN) Total Score

End point description:

NAPPA is a clinical and participant-reported outcomes tool, and consists of 3 components: a questionnaire assessing nail-specific quality of life NAPPA-QoL (Nail Assessment in Psoriasis and Psoriatic Arthritis Quality of Life), a 2-part questionnaire assessing participant relevant needs and treatment benefits NAPPA-PBI (Nail Assessment in Psoriasis and Psoriatic Arthritis – Patient Benefit Index), and a clinical assessment of objective finger nail psoriasis severity NAPPA-CLIN. Sum of all assessed finger and toes ranging between 0 (no involvement) to 16 (worst involvement). LS mean change from baseline was calculated using ANCOVA with mBOCF and with terms for baseline and treatment.

APD: All randomized participants who had palmoplantar, scalp, or nail involvement at baseline.
mBOCF: Participants who discontinued treatment due to AE were imputed by their baseline observation, Participants who discontinued due to other reasons were imputed by their last observation.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	29	27	
Units: units on a scale				
least squares mean (confidence interval 95%)	-6.58 (-8.12 to -5.04)	-0.14 (-1.91 to 1.62)	-3.41 (-5.30 to -1.52)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in European Quality of Life - 5 Dimensions 5 Level (EQ-5D) + Bolt On UK population-based index score

End point title	Change from Baseline in European Quality of Life - 5 Dimensions 5 Level (EQ-5D) + Bolt On UK population-based index score

End point description:

The European Quality of Life - 5 Dimensions 5 Level (EQ-5D-5L) is a standardized measure of health status used to provide a simple, generic measure of health for clinical and economic appraisal. The EQ-5D-5L consists of a descriptive system of the respondent's health which comprises the following 5 dimensions: 1) mobility 2) self-care 3) usual activities 4) pain/discomfort 5) anxiety/depression. The EQ-5D-5L health states were converted into a single summary index by applying a crosswalk using a United Kingdom (UK) Population value set to each of the levels in each dimension. This produced participant-level index scores between -0.594 and 1.0 (worse to better health). LS mean change from baseline was calculated using ANCOVA with mBOCF and with terms for baseline and treatment.
APD: All randomized participants who received at least 1 dose of study drug and had baseline and a post-baseline measurement for EQ-5D 5L Index.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	47	50	
Units: units on a scale				
least squares mean (confidence interval 95%)	0.15 (0.11 to 0.20)	0.04 (-0.01 to 0.09)	0.15 (0.10 to 0.20)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in European Quality of Life - 5 Dimensions 5 Level (EQ-5D 5L) "Bolt On" - Psoriasis (PSO) index score

End point title	Change From Baseline in European Quality of Life - 5 Dimensions 5 Level (EQ-5D 5L) "Bolt On" - Psoriasis (PSO) index score

End point description:

The European Quality of Life - 5 Dimensions 5 Level (EQ-5D-5L) is a standardized measure of health status used to provide a simple, generic measure of health for clinical and economic appraisal. The EQ-5D-5L consists of a descriptive system of the respondent's health which comprises the following 5 dimensions: 1) mobility 2) self-care 3) usual activities 4) pain/discomfort 5) anxiety/depression. The Bolt On PSO is an addition to the EQ-5D-5L that consists of 2 dimensions specific to psoriatic disease: 6) skin irritation (itching) and 7) self-confidence. Index scores for the Bolt On PSO range from 0.0042 to 1.0 (worse to better health). LS mean change from baseline was calculated using ANCOVA with mBOCF and with terms for baseline and treatment.
APD: All randomized participants who received at least 1 dose of study drug and had baseline and a post-baseline measurement for EQ-5D 5L "Bolt On" PSO-Index.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	46	50	
Units: units on a scale				
least squares mean (confidence interval 95%)	0.15 (0.12 to 0.18)	0.05 (0.01 to 0.08)	0.13 (0.10 to 0.16)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in European Quality of Life - 5 Dimensions 5 Level (EQ-5D 5L) "Bolt On" - Visual Analog Scale Score

End point title	Change From Baseline in European Quality of Life - 5 Dimensions 5 Level (EQ-5D 5L) "Bolt On" - Visual Analog Scale Score

End point description:

The EQ-5D 5L is a standardized measure of health status that includes a descriptive system of the respondent's health and a rating of his/her current health state using a 0 (worst health imaginable)- to 100 (best health imaginable)-millimeter (mm) Visual Analog Scale (VAS). LS mean change from baseline was calculated using ANCOVA with mBOCF and with terms for baseline and treatment.

APD: All randomized participants who received at least 1 dose of study drug and had baseline and a post-baseline measurement for EQ-5D 5L + Bolt on VAS.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	48	50	
Units: Millimeter (mm)				
least squares mean (confidence interval 95%)	16.91 (12.23 to 21.59)	6.08 (1.21 to 10.96)	13.91 (9.14 to 18.69)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on the Work Productivity Activity Impairment Questionnaire-Psoriasis (WPAI-PSO), Absenteeism score

End point title	Change From Baseline on the Work Productivity Activity Impairment Questionnaire-Psoriasis (WPAI-PSO), Absenteeism score

End point description:

The WPAI-PSO consists of 6 questions to determine employment status, hours missed from work because of psoriasis, hours missed from work for other reasons, hours actually worked, the degree to

which psoriasis affected work productivity while at work, and the degree to which psoriasis affected activities outside of work. 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. Each WPAI score is expressed as impairment percentages (0-100), where 0 (no impairement) and 100 (greater impairment). LS mean change from baseline was calculated using ANCOVA with mBOCF and with terms for baseline and treatment.

APD: All randomized participants who received at least 1 dose of study drug and had baseline and a post-baseline measurement for WPAI-PSO absenteeism score.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	30	39	
Units: units on a scale				
least squares mean (confidence interval 95%)	3.08 (-3.79 to 9.96)	-1.26 (-7.69 to 5.17)	0.06 (-5.49 to 5.62)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on the Work Productivity Activity Impairment Questionnaire-Psoriasis (WPAI-PSO), Presenteeism Score

End point title	Change From Baseline on the Work Productivity Activity Impairment Questionnaire-Psoriasis (WPAI-PSO), Presenteeism Score

End point description:

The WPAI-PSO consists of 6 questions to determine employment status, hours missed from work because of psoriasis, hours missed from work for other reasons, hours actually worked, the degree to which psoriasis affected work productivity while at work, and the degree to which psoriasis affected activities outside of work. 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. Each WPAI score is expressed as impairment percentages (0-100), where 0 (no impairement) and 100 (greater impairment). LS mean change from baseline was calculated using ANCOVA with mBOCF and with terms for baseline and treatment.

APD: All randomized participants who received at least 1 dose of study drug and had baseline and a post-baseline measurement for WPAI-PSO Presenteeism score.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29	32	39	
Units: units on a scale				
least squares mean (confidence interval 95%)	-22.70 (-28.73 to -16.66)	-5.29 (-11.10 to 0.52)	-20.32 (-25.51 to -15.13)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on the Work Productivity Activity Impairment Questionnaire-Psoriasis (WPAI-PSO), Impairment in Activities Performed Outside of Work

End point title	Change From Baseline on the Work Productivity Activity Impairment Questionnaire-Psoriasis (WPAI-PSO), Impairment in Activities Performed Outside of Work

End point description:

The WPAI-PSO consists of 6 questions to determine employment status, hours missed from work because of psoriasis, hours missed from work for other reasons, hours actually worked, the degree to which psoriasis affected work productivity while at work, and the degree to which psoriasis affected activities outside of work. 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. Each WPAI score is expressed as impairment percentages (0-100), where 0 (no impairement) and 100 (greater impairment). LS mean change from baseline was calculated using ANCOVA with mBOCF and with terms for baseline and treatment.

APD: All randomized participants who received at least 1 dose of study drug and had baseline and a post-baseline measurement for WPAI-PSO.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	50	48	
Units: units on a scale				
least squares mean (confidence interval 95%)	-28.23 (-33.99 to -22.47)	-3.45 (-9.38 to 2.47)	-23.57 (-29.58 to -17.55)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on the Work Productivity Activity Impairment Questionnaire-Psoriasis (WPAI-PSO), Overall Work Impairment Score

End point title	Change From Baseline on the Work Productivity Activity Impairment Questionnaire-Psoriasis (WPAI-PSO), Overall Work Impairment Score

End point description:

The WPAI-PSO consists of 6 questions to determine employment status, hours missed from work because of psoriasis, hours missed from work for other reasons, hours actually worked, the degree to which psoriasis affected work productivity while at work, and the degree to which psoriasis affected activities outside of work. 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. Each WPAI score is expressed as impairment percentages (0-100), where 0 (no impairement) and 100 (greater impairment). LS mean change from baseline was calculated using ANCOVA with mBOCF and with terms for baseline and treatment.

APD: All randomized participants who received at least 1 dose of study drug and had baseline and a post-baseline measurement for WPAI-PSO.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25	30	38	
Units: units on a scale				
least squares mean (confidence interval 95%)	-18.20 (-26.29 to -10.11)	-6.20 (-13.66 to 1.27)	-19.80 (-26.31 to -13.29)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Positive Responses to Neck/Face Psoriasis Question

End point title	Percentage of Participants with Positive Responses to Neck/Face Psoriasis Question

End point description:

Studying psoriasis involvement in the face, neck, and the genitals is of considerable interest for participants. These are locations that bear high potential for stigmatization and/or psychological distress, and, hence, effects in those regions are assumed to heavily influence participant's quality of life. Following set of binary questions were asked to check the satisfaction of participants. 1) Does the participant currently have visible psoriasis on face/neck? (Yes/No) 2) Does the participant currently have psoriasis on the genital area? (Yes/No).

APD: All randomized participants who received at least 1 dose of study drug and had baseline and a post-baseline measurement for binary questions.
Participants who did not meet the clinical response criteria or had missing data were considered non-responders for Non-Responder Imputation (NRI) analysis.

End point type	Secondary

End point timeframe:

Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	34	36	
Units: Percentage of Participants				
number (not applicable)	81.8	26.5	66.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants positive responses to genital psoriasis question

End point title	Percentage of Participants positive responses to genital psoriasis question

End point description:

Studying psoriasis involvement in the face, neck, and the genitals is of considerable interest for participants. These are locations that bear high potential for stigmatization and/or psychological distress, and, hence, effects in those regions are assumed to heavily influence participant's quality of life. Following set of binary questions were asked to check the satisfaction of participants. 1) Does the patient currently have visible psoriasis on face/neck? (Yes/No) 2) Does the patient currently have psoriasis on the genital area? (Yes/No) The genital area includes the labia majora (hair-bearing), labia minora modified mucus membrane, and perineum in female patients; and the penis glans, penis – shaft, and scrotum in male patients.
APD:All randomized participants who received at least 1 dose of study drug and had baseline and a post-baseline measurement for binary questions.
Participants who did not meet the clinical response criteria or had missing data were considered NRI analys

End point type	Secondary

End point timeframe:

Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	24	24	
Units: Percentage of participants				
number (not applicable)	85.0	29.2	75.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean adherence on medication and satisfaction with therapy (STAQ)

End point title	Mean adherence on medication and satisfaction with therapy (STAQ)

End point description:

STAQ is a 38 item questionnaire that was developed by shortening and adapting the Topical Treatment Adherence Questionnaire (TTAQ) for administration to participants under systemic therapy. The following STAQ items are of special interest for this study. 1) STAQ item 13 (The treatment does not affect my sex life) 2) STAQ item 16 (I am enjoying life again as a result of the treatment) 3) STAQ item 20 (The side effects of the treatment were acceptable) 4) STAQ item 31 (I am satisfied with the efficacy of the treatment) 5) STAQ item 32 (I am satisfied with the tolerability of the treatment) 6) STAQ item 35 (The positive aspects of the treatment outweigh the negative ones). The STAQ items are on a 4-point Likert scale with scores between 0 (strong disagreement) and 3 (strong agreement). LS mean was calculated using ANCOVA with term for treatment.
APD: All randomized participants who received at least 1 dose of study drug and had a post-baseline measurement for STAQ.

End point type	Secondary

End point timeframe:

Week 24

End point values	Ixekizumab	Fumaric Acid Esters	Methotrexate	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	22	48	
Units: units on a scale				
least squares mean (confidence interval 95%)				
STAQ item 13|	2.84 (2.68 to 3.00)	2.75 (2.51 to 2.99)	2.78 (2.61 to 2.94)	
STAQ item 16|	2.82 (2.60 to 3.04)	2.00 (1.68 to 2.32)	2.43 (2.20 to 2.66)	
STAQ item 20|	2.76 (2.51 to 3.01)	2.00 (1.66 to 2.34)	2.42 (2.17 to 2.66)	
STAQ item 31|	2.88 (2.68 to 3.08)	2.09 (1.79 to 2.39)	2.29 (2.09 to 2.50)	
STAQ item 32|	2.86 (2.66 to 3.05)	1.95 (1.66 to 2.25)	2.50 (2.30 to 2.70)	
STAQ item 35|	2.80 (2.58 to 3.02)	2.14 (1.82 to 2.46)	2.53 (2.31 to 2.75)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Entire Study	
Adverse event reporting additional description:	
All randomized participants.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups	
Reporting group title	Ixekizumab-Treatment Period
Reporting group description: -	
Reporting group title	Fumaric Acid Esters-Treatment Period
Reporting group description: -	
Reporting group title	Methotrexate-Treatment Period
Reporting group description: -	
Reporting group title	Fumaric Acid Esters-Extension Period
Reporting group description: -	
Reporting group title	Methotrexate-Extension Period
Reporting group description: -	
Reporting group title	Ixekizumab-Extension Period
Reporting group description: -	
Reporting group title	Follow-up period
Reporting group description: -	

Serious adverse events	Ixekizumab-Treatment Period	Fumaric Acid Esters-Treatment Period	Methotrexate-Treatment Period
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 54 (1.85%)	3 / 52 (5.77%)	1 / 52 (1.92%)
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)			
anogenital warts			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (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
invasive lobular breast carcinoma			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (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
pancreatic neuroendocrine tumour			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (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 19.1			
subjects affected / exposed	1 / 54 (1.85%)	0 / 52 (0.00%)	0 / 52 (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
Nervous system disorders			
sciatica			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (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			
lymphadenopathy			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
colitis			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	0 / 54 (0.00%)	1 / 52 (1.92%)	0 / 52 (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
gastritis erosive			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
hepatic cirrhosis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (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			
tonsillar hypertrophy			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (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			
intervertebral disc protrusion			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	1 / 52 (1.92%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
osteoarthritis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
erysipelas			

alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	1 / 52 (1.92%)	0 / 52 (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
gastroenteritis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (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
infected dermal cyst			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (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	Fumaric Acid Esters-Extension Period	Methotrexate-Extension Period	Ixekizumab-Extension Period
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 19 (5.26%)	4 / 31 (12.90%)	3 / 48 (6.25%)
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)			
anogenital warts			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 19 (0.00%)	1 / 31 (3.23%)	0 / 48 (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
invasive lobular breast carcinoma			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 19 (0.00%)	0 / 31 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pancreatic neuroendocrine tumour			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	0 / 19 (0.00%)	0 / 31 (0.00%)	1 / 48 (2.08%)
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 19.1			
subjects affected / exposed	0 / 19 (0.00%)	0 / 31 (0.00%)	0 / 48 (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			
sciatica			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 19 (0.00%)	0 / 31 (0.00%)	0 / 48 (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			
lymphadenopathy			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 19 (0.00%)	0 / 31 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 19 (0.00%)	0 / 31 (0.00%)	0 / 48 (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
colitis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 19 (0.00%)	0 / 31 (0.00%)	0 / 48 (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 erosive			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	0 / 19 (0.00%)	0 / 31 (0.00%)	0 / 48 (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			
hepatic cirrhosis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 19 (0.00%)	0 / 31 (0.00%)	0 / 48 (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			
tonsillar hypertrophy			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 19 (0.00%)	1 / 31 (3.23%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
intervertebral disc protrusion			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 19 (0.00%)	0 / 31 (0.00%)	1 / 48 (2.08%)
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 19.1			
subjects affected / exposed	0 / 19 (0.00%)	2 / 31 (6.45%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
erysipelas			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 19 (0.00%)	0 / 31 (0.00%)	0 / 48 (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 19.1			
subjects affected / exposed	0 / 19 (0.00%)	0 / 31 (0.00%)	0 / 48 (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
infected dermal cyst			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	0 / 31 (0.00%)	0 / 48 (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	Follow-up period		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 113 (3.54%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
anogenital warts			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
invasive lobular breast carcinoma			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
pancreatic neuroendocrine tumour			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
atrioventricular block complete			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	0 / 113 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
sciatica			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
lymphadenopathy			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
colitis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
gastritis erosive			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
hepatic cirrhosis			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
tonsillar hypertrophy			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
intervertebral disc protrusion			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
osteoarthritis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
erysipelas			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
gastroenteritis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
infected dermal cyst			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	0 / 113 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Ixekizumab-Treatment Period	Fumaric Acid Esters-Treatment Period	Methotrexate-Treatment Period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 54 (68.52%)	39 / 52 (75.00%)	38 / 52 (73.08%)
Vascular disorders			
flushing			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	13 / 52 (25.00%)	0 / 52 (0.00%)
occurrences (all)	0	19	0
haematoma			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 54 (1.85%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
fatigue			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	4 / 54 (7.41%)	3 / 52 (5.77%)	8 / 52 (15.38%)
occurrences (all)	4	3	14
injection site erythema			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
injection site pruritus			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
injection site reaction			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	7 / 54 (12.96%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences (all)	23	0	0
injection site swelling			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
bronchial hyperreactivity			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
cough			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 54 (1.85%)	2 / 52 (3.85%)	1 / 52 (1.92%)
occurrences (all)	1	2	1
oropharyngeal pain			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	3 / 54 (5.56%)	1 / 52 (1.92%)	1 / 52 (1.92%)
occurrences (all)	3	1	1
Investigations			
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
gamma-glutamyltransferase increased			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	3 / 52 (5.77%)	0 / 52 (0.00%)
occurrences (all)	0	3	0
weight increased			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 54 (1.85%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			

arthropod bite			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	3 / 52 (5.77%)
occurrences (all)	0	0	3
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	2 / 54 (3.70%)	0 / 52 (0.00%)	1 / 52 (1.92%)
occurrences (all)	2	0	1
headache			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	7 / 54 (12.96%)	4 / 52 (7.69%)	9 / 52 (17.31%)
occurrences (all)	7	4	12
Blood and lymphatic system disorders			
lymphopenia			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	5 / 52 (9.62%)	2 / 52 (3.85%)
occurrences (all)	0	5	2
Ear and labyrinth disorders			
middle ear inflammation			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
vertigo			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	2 / 54 (3.70%)	3 / 52 (5.77%)	3 / 52 (5.77%)
occurrences (all)	2	3	5
Gastrointestinal disorders			
abdominal pain upper			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	2 / 54 (3.70%)	19 / 52 (36.54%)	6 / 52 (11.54%)
occurrences (all)	2	26	6
diarrhoea			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 54 (1.85%)	24 / 52 (46.15%)	6 / 52 (11.54%)
occurrences (all)	1	29	6

dyspepsia			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
flatulence			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	3 / 52 (5.77%)	0 / 52 (0.00%)
occurrences (all)	0	3	0
nausea			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 54 (1.85%)	3 / 52 (5.77%)	5 / 52 (9.62%)
occurrences (all)	1	4	14
oral mucosal eruption			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
vomiting			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	3 / 52 (5.77%)	0 / 52 (0.00%)
occurrences (all)	0	4	0
Skin and subcutaneous tissue disorders			
alopecia			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	2 / 54 (3.70%)	0 / 52 (0.00%)	1 / 52 (1.92%)
occurrences (all)	2	0	1
dermatitis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
eczema			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
ingrowing nail			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	0 / 54 (0.00%)	1 / 52 (1.92%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
nail psoriasis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
night sweats			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	1 / 52 (1.92%)
occurrences (all)	0	0	1
xanthelasma			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	2 / 54 (3.70%)	0 / 52 (0.00%)	4 / 52 (7.69%)
occurrences (all)	2	0	6
back pain			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 54 (1.85%)	2 / 52 (3.85%)	5 / 52 (9.62%)
occurrences (all)	1	2	5
bursitis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
musculoskeletal pain			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
myalgia			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	1 / 52 (1.92%)
occurrences (all)	0	0	1
pain in extremity			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 54 (1.85%)	1 / 52 (1.92%)	0 / 52 (0.00%)
occurrences (all)	1	1	0
Infections and infestations			
bronchitis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 54 (1.85%)	1 / 52 (1.92%)	1 / 52 (1.92%)
occurrences (all)	1	1	1
gastroenteritis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 54 (1.85%)	1 / 52 (1.92%)	0 / 52 (0.00%)
occurrences (all)	1	1	0
impetigo			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
nasopharyngitis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	20 / 54 (37.04%)	9 / 52 (17.31%)	18 / 52 (34.62%)
occurrences (all)	23	13	21
sinusitis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	1 / 52 (1.92%)	1 / 52 (1.92%)
occurrences (all)	0	1	1
tinea pedis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	2 / 54 (3.70%)	0 / 52 (0.00%)	1 / 52 (1.92%)
occurrences (all)	2	0	1
tooth infection			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
hyperlipidaemia			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 54 (0.00%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Fumaric Acid Esters-Extension Period	Methotrexate-Extension Period	Ixekizumab-Extension Period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 19 (78.95%)	18 / 31 (58.06%)	24 / 48 (50.00%)
Vascular disorders			
flushing			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 19 (0.00%)	0 / 31 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
haematoma			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	0 / 31 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
fatigue			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	0 / 31 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
injection site erythema			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	2 / 19 (10.53%)	3 / 31 (9.68%)	0 / 48 (0.00%)
occurrences (all)	10	13	0
injection site pruritus			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	1 / 31 (3.23%)	0 / 48 (0.00%)
occurrences (all)	3	1	0
injection site reaction			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	3 / 19 (15.79%)	6 / 31 (19.35%)	1 / 48 (2.08%)
occurrences (all)	6	31	9
injection site swelling			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	2 / 19 (10.53%)	3 / 31 (9.68%)	0 / 48 (0.00%)
occurrences (all)	10	9	0
Respiratory, thoracic and mediastinal disorders			
bronchial hyperreactivity			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	0 / 31 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
cough			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	0 / 31 (0.00%)	1 / 48 (2.08%)
occurrences (all)	1	0	1
oropharyngeal pain			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	0 / 31 (0.00%)	1 / 48 (2.08%)
occurrences (all)	1	0	1
Investigations			
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	1 / 31 (3.23%)	0 / 48 (0.00%)
occurrences (all)	1	1	0
gamma-glutamyltransferase increased			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 19 (0.00%)	0 / 31 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
weight increased			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 19 (0.00%)	2 / 31 (6.45%)	0 / 48 (0.00%)
occurrences (all)	0	2	0
Injury, poisoning and procedural complications			

arthropod bite			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 19 (0.00%)	0 / 31 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	0 / 31 (0.00%)	1 / 48 (2.08%)
occurrences (all)	1	0	1
headache			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	2 / 31 (6.45%)	1 / 48 (2.08%)
occurrences (all)	1	2	1
Blood and lymphatic system disorders			
lymphopenia			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	0 / 31 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
middle ear inflammation			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	0 / 31 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
vertigo			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 19 (0.00%)	0 / 31 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
abdominal pain upper			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 19 (0.00%)	0 / 31 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
diarrhoea			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	1 / 31 (3.23%)	1 / 48 (2.08%)
occurrences (all)	1	1	1

dyspepsia			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	0 / 31 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
flatulence			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	0 / 31 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
nausea			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	0 / 31 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
oral mucosal eruption			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	0 / 31 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
vomiting			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 19 (0.00%)	0 / 31 (0.00%)	1 / 48 (2.08%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
alopecia			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 19 (0.00%)	2 / 31 (6.45%)	0 / 48 (0.00%)
occurrences (all)	0	2	0
dermatitis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	0 / 31 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
eczema			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	2 / 19 (10.53%)	2 / 31 (6.45%)	2 / 48 (4.17%)
occurrences (all)	2	2	4
ingrowing nail			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	1 / 19 (5.26%)	0 / 31 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
nail psoriasis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	0 / 31 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
night sweats			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	0 / 31 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
xanthelasma			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	0 / 31 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 19 (0.00%)	2 / 31 (6.45%)	1 / 48 (2.08%)
occurrences (all)	0	2	1
back pain			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 19 (0.00%)	0 / 31 (0.00%)	3 / 48 (6.25%)
occurrences (all)	0	0	3
bursitis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 19 (0.00%)	2 / 31 (6.45%)	0 / 48 (0.00%)
occurrences (all)	0	2	0
musculoskeletal pain			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	0 / 31 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
myalgia			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	2 / 19 (10.53%)	0 / 31 (0.00%)	0 / 48 (0.00%)
occurrences (all)	4	0	0
pain in extremity			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	1 / 31 (3.23%)	1 / 48 (2.08%)
occurrences (all)	1	1	1
Infections and infestations			
bronchitis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	0 / 31 (0.00%)	2 / 48 (4.17%)
occurrences (all)	1	0	2
gastroenteritis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 19 (0.00%)	2 / 31 (6.45%)	2 / 48 (4.17%)
occurrences (all)	0	2	2
impetigo			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	0 / 31 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
nasopharyngitis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	6 / 19 (31.58%)	10 / 31 (32.26%)	18 / 48 (37.50%)
occurrences (all)	7	15	25
sinusitis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	0 / 31 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
tinea pedis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	2 / 19 (10.53%)	0 / 31 (0.00%)	1 / 48 (2.08%)
occurrences (all)	2	0	1
tooth infection			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	1 / 19 (5.26%)	0 / 31 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
hyperlipidaemia			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 19 (5.26%)	0 / 31 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Follow-up period		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 113 (0.00%)		
Vascular disorders			
flushing			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
haematoma			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
fatigue			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
injection site erythema			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
injection site pruritus			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
injection site reaction			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
injection site swelling			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
bronchial hyperreactivity			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
cough			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
oropharyngeal pain			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
Investigations			
aspartate aminotransferase increased			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
gamma-glutamyltransferase increased			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
weight increased			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			

arthropod bite alternative dictionary used: MedDRA 19.1 subjects affected / exposed occurrences (all)	0 / 113 (0.00%) 0		
Nervous system disorders dizziness alternative dictionary used: MedDRA 19.1 subjects affected / exposed occurrences (all)	0 / 113 (0.00%) 0		
headache alternative dictionary used: MedDRA 19.1 subjects affected / exposed occurrences (all)	0 / 113 (0.00%) 0		
Blood and lymphatic system disorders lymphopenia alternative dictionary used: MedDRA 19.1 subjects affected / exposed occurrences (all)	0 / 113 (0.00%) 0		
Ear and labyrinth disorders middle ear inflammation alternative dictionary used: MedDRA 19.1 subjects affected / exposed occurrences (all)	0 / 113 (0.00%) 0		
vertigo alternative dictionary used: MedDRA 19.1 subjects affected / exposed occurrences (all)	0 / 113 (0.00%) 0		
Gastrointestinal disorders abdominal pain upper alternative dictionary used: MedDRA 19.1 subjects affected / exposed occurrences (all)	0 / 113 (0.00%) 0		
diarrhoea alternative dictionary used: MedDRA 19.1 subjects affected / exposed occurrences (all)	0 / 113 (0.00%) 0		

dyspepsia			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
flatulence			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
nausea			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
oral mucosal eruption			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
vomiting			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
alopecia			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
dermatitis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
eczema			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
ingrowing nail			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
nail psoriasis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
night sweats			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
xanthelasma			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
back pain			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
bursitis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
musculoskeletal pain			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
myalgia			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
pain in extremity			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
Infections and infestations			
bronchitis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
gastroenteritis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
impetigo			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
nasopharyngitis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
sinusitis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
tinea pedis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 113 (0.00%)		
occurrences (all)	0		
tooth infection			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed occurrences (all)	0 / 113 (0.00%) 0		
Metabolism and nutrition disorders hyperlipidaemia alternative dictionary used: MedDRA 19.1 subjects affected / exposed occurrences (all)	 0 / 113 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 November 2015	Amendment (b): Amended to include a statement on dose reduction for fumaderm and methotrexate.
07 April 2016	Amendment (c): Amended to provide outcome description and scale details for Columbia Suicide Severity Rating Scale and Quick Inventory of Depressive Symptomatology-Self Report (16 items) (QIDS-SR16).
07 June 2016	Amendment (d): Amended study design at Week 24.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported