Clinical trial results:
A 52-Week Multicenter, Randomized, Blinded,Parallel-Group Study Comparing the Efficacy and Safety of Ixekizumab to Ustekinumab in Patients with Moderate-to-Severe Plaque Psoriasis.

Summary

EudraCT number	2015-000892-28
Trial protocol	DE GB SE HU NL ES AT BE PL IT
Global end of trial date	05 October 2017

Results information

Result version number	v1 (current)
This version publication date	14 October 2018
First version publication date	14 October 2018

Trial information

Trial identification

Sponsor protocol code	I1F-MC-RHBS

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02561806
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 16012

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, United States, 46285
Public contact	1-877-CTLILLY (1-877-285-4559) or, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Mon - Fri 9 AM - 5 PM Eastern time (UTC/GMT - 5 hours, 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	05 October 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 October 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 of the study drug ixekizumab compared to ustekinumab in participants with moderate-to-severe-plaque psoriasis.

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

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Hungary: 23
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Switzerland: 11
Country: Number of subjects enrolled	Spain: 25
Country: Number of subjects enrolled	Canada: 52
Country: Number of subjects enrolled	Austria: 12
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Sweden: 6
Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	Poland: 38
Country: Number of subjects enrolled	Italy: 8
Country: Number of subjects enrolled	France: 48
Country: Number of subjects enrolled	Germany: 66
Worldwide total number of subjects	302
EEA total number of subjects	239

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)	286
From 65 to 84 years	16
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Induction period occurring from week 0 to week 12 followed by maintenance period occurring week 12 to week 52 followed by post-treatment follow-up period occurring from last treatment period visit (week 52) or Early termination visit, for a minimum of 12 weeks following that visit.

Pre-assignment

Screening details:

Screening occurred approximately 4 to 35 days before induction period, Screening procedures (including complete medical history and demographics) were performed.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Ustekinumab

Arm description:

45 milligram (mg) ustekinumab given as subcutaneous (SC) injection for participants ≤100 kilograms (kg) and 90 mg SC injection for participants >100 kg at Week 0, 4, 16, 28, and 40. Placebo for ixekizumab injections was used for blinding.

Arm type	Active comparator
Investigational medicinal product name	Ustekinumab
Investigational medicinal product code	
Other name	Stelara
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

45 milligram (mg) Ustekinumab given as subcutaneous (SC) injection for participants ≤100 kilograms (kg) and 90 mg SC injection for participants >100 kg at Week 0, 4, 16, 28, and 40.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo administered subcutaneously.

Arm title	Ixekizumab

Arm description:

160 mg ixekizumab given as two subcutaneous (SC) injections at baseline followed by 80 mg ixekizumab given as a single SC injection once every 2 weeks from week 2 through week 12. After week 12 participants will receive 80 mg ixekizumab every 4 weeks through week 52. Placebo for ustekinumab injections was used for blinding.

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) injections at baseline followed by 80 mg Ixekizumab given as a single SC injection once every 2 weeks from week 2 through week 12. After week 12 participants will receive 80 mg Ixekizumab every 4 weeks through week 52.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo administered subcutaneously.

Number of subjects in period 1	Ustekinumab	Ixekizumab
Started	166	136
Received At least one dose of study drug	166	135
Completed	164	131
Not completed	2	5
Consent withdrawn by subject	-	2
Adverse event, non-fatal	-	2
Randomized but not treated	-	1
Site staff became unblinded	1	-
Lack of efficacy	1	-

Period 2

Period 2 title	Maintenance Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes

Arm title	Ustekinumab

Arm description:

45 milligram (mg) ustekinumab given as subcutaneous (SC) injection for participants ≤100 kilograms (kg) and 90 mg SC injection for participants >100 kg at Week 0, 4, 16, 28, and 40. Placebo for ixekizumab injections was used for blinding.

Arm type	Active comparator
Investigational medicinal product name	Ustekinumab
Investigational medicinal product code	
Other name	Stelara
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

45 milligram (mg) Ustekinumab given as subcutaneous (SC) injection for participants ≤100 kilograms (kg) and 90 mg SC injection for participants >100 kg at Week 0, 4, 16, 28, and 40.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo administered subcutaneously.

Arm title	Ixekizumab

Arm description:

160 mg ixekizumab given as two subcutaneous (SC) injections at baseline followed by 80 mg ixekizumab given as a single SC injection once every 2 weeks from week 2 through week 12. After week 12 participants will receive 80 mg ixekizumab every 4 weeks through week 52. Placebo for ustekinumab injections was used for blinding.

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) injections at baseline followed by 80 mg Ixekizumab given as a single SC injection once every 2 weeks from week 2 through week 12. After week 12 participants will receive 80 mg Ixekizumab every 4 weeks through week 52.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo administered subcutaneously.

Number of subjects in period 2	Ustekinumab	Ixekizumab
Started	164	131
Completed	151	123
Not completed	13	8
Consent withdrawn by subject	5	3
Adverse event, non-fatal	2	1
Site staff became unblinded	-	1
Lost to follow-up	2	2
Lack of efficacy	3	1
Protocol deviation	1	-

Period 3	
Period 3 title	Post-Treatment Follow-up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Ustekinumab

Arm description:

Participants were allowed to continue the treatment administered during the blinded period or any other psoriasis treatment.

Arm type	Allowed to continue any other psoriasis treatment

No investigational medicinal product assigned in this arm

Arm title	Ixekizumab

Arm description:

Participants were allowed to continue the treatment administered during the blinded period or any other psoriasis treatment.

Arm type	Allowed to continue any other psoriasis treatment

No investigational medicinal product assigned in this arm

Number of subjects in period 3[1]	Ustekinumab	Ixekizumab
Started	157	60
Completed	155	59
Not completed	2	1
Consent withdrawn by subject	1	-
Lost to follow-up	1	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 follow-up period.

Baseline characteristics

Reporting groups	
Reporting group title	Ustekinumab
Reporting group description:	
45 milligram (mg) ustekinumab given as subcutaneous (SC) injection for participants ≤100 kilograms (kg) and 90 mg SC injection for participants >100 kg at Week 0, 4, 16, 28, and 40. Placebo for ixekizumab injections was used for blinding.	
Reporting group title	Ixekizumab
Reporting group description:	
160 mg ixekizumab given as two subcutaneous (SC) injections at baseline followed by 80 mg ixekizumab given as a single SC injection once every 2 weeks from week 2 through week 12. After week 12 participants will receive 80 mg ixekizumab every 4 weeks through week 52. Placebo for ustekinumab injections was used for blinding.	

Reporting group values	Ustekinumab	Ixekizumab	Total
Number of subjects	166	136	302
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	44	42.7	
standard deviation	± 13.25	± 12.67	-
Gender categorical Units: Subjects			
Female	54	46	100
Male	112	90	202
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	5	4	9
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	3	4
White	157	125	282
More than one race	1	2	3
Unknown or Not Reported	2	2	4
Region of Enrollment Units: Subjects			
Hungary	12	11	23

United Kingdom	4	2	6
Switzerland	6	5	11
Spain	13	12	25
Canada	27	25	52
Austria	6	6	12
Netherlands	0	1	1
Sweden	4	2	6
Belgium	4	2	6
Poland	21	17	38
Italy	4	4	8
France	25	23	48
Germany	40	26	66
Age group at psoriasis onset Units: Subjects			
<40 years (Type 1 psoriasis)	134	113	247
>=40 years (Type 2 psoriasis)	32	23	55
Weight Units: Kilogram			
arithmetic mean	89.4	85.8	
standard deviation	± 24.5	± 20.30	-
BMI Units: kg/m^2			
arithmetic mean	29.7	28.8	
standard deviation	± 6.97	± 5.55	-
Duration of psoriasis Units: years			
arithmetic mean	18.2	18.0	
standard deviation	± 12.0	± 11.14	-
Psoriasis Area & Severity Index (PASI)			
PASI combines the extent of body surface involvement in 4 anatomical regions (head, trunk, arms, & legs). For each region the % area of skin involved was estimated from 0(0%) to 6(90%-100%) & severity was estimated by clinical signs of erythema, induration & scaling with scores range from 0 to 4 ("no" to "severe" involvement). Each area is scored & scores were combined for final PASI (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 (most severe disease).			
Units: units on a scale			
arithmetic mean	19.8	19.9	
standard deviation	± 9.02	± 8.15	-

End points

End points reporting groups

Reporting group title	Ustekinumab

Reporting group description:

45 milligram (mg) ustekinumab given as subcutaneous (SC) injection for participants ≤100 kilograms (kg) and 90 mg SC injection for participants >100 kg at Week 0, 4, 16, 28, and 40. Placebo for ixekizumab injections was used for blinding.

Reporting group title	Ixekizumab

Reporting group description:

160 mg ixekizumab given as two subcutaneous (SC) injections at baseline followed by 80 mg ixekizumab given as a single SC injection once every 2 weeks from week 2 through week 12. After week 12 participants will receive 80 mg ixekizumab every 4 weeks through week 52. Placebo for ustekinumab injections was used for blinding.

Reporting group title	Ustekinumab

Reporting group description:

45 milligram (mg) ustekinumab given as subcutaneous (SC) injection for participants ≤100 kilograms (kg) and 90 mg SC injection for participants >100 kg at Week 0, 4, 16, 28, and 40. Placebo for ixekizumab injections was used for blinding.

Reporting group title	Ixekizumab

Reporting group description:

160 mg ixekizumab given as two subcutaneous (SC) injections at baseline followed by 80 mg ixekizumab given as a single SC injection once every 2 weeks from week 2 through week 12. After week 12 participants will receive 80 mg ixekizumab every 4 weeks through week 52. Placebo for ustekinumab injections was used for blinding.

Reporting group title	Ustekinumab

Reporting group description:

Participants were allowed to continue the treatment administered during the blinded period or any other psoriasis treatment.

Reporting group title	Ixekizumab

Reporting group description:

Participants were allowed to continue the treatment administered during the blinded period or any other psoriasis treatment.

Primary: 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 by itself and the scores were 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: All randomized participants who received at least 1 dose of study drug and had baseline and 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	Primary

End point timeframe:

Week 12

End point values	Ustekinumab	Ixekizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	166	136		
Units: percentage of participants				
number (not applicable)	42.2	72.8		

Statistical analyses

Statistical analysis title	STATISTICAL ANALYSIS 1
Comparison groups	Ustekinumab v Ixekizumab
Number of subjects included in analysis	302
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Risk difference (RD)
Point estimate	0.321
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.198
upper limit	0.445

Secondary: Percentage of Participants with a ≥75% Improvement in PASI (PASI 75) from Baseline

End point title	Percentage of Participants with a ≥75% Improvement in PASI (PASI 75) 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 by itself 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: All randomized participants who received at least 1 dose of study drug and had a post-baseline measurement for PASI 75. Participants who did not meet the clinical response criteria or had missing data at Week 12 were considered non-responders for Non-Responder Imputation (NRI) analysis.

End point type	Secondary

End point timeframe:

Week 12

End point values	Ustekinumab	Ixekizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	166	136		
Units: percentage of participants				
number (not applicable)	68.7	88.2		

Statistical analyses

Statistical analysis title	STATISTICAL ANALYSIS 1
Comparison groups	Ustekinumab v Ixekizumab
Number of subjects included in analysis	302
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Risk ratio (RR)
Point estimate	1.285
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.13
upper limit	1.439

Secondary: Percentage of Participants with a 100% Improvement of PASI (PASI 100) from Baseline

End point title	Percentage of Participants with a 100% Improvement of PASI (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 by itself and the scores were 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: All randomized participants who received at least 1 dose of study drug and had a post-baseline measurement for PASI 100. Participants who did not meet the clinical response criteria or had missing data at Week 12 were considered non-responders for Non-Responder Imputation (NRI) analysis.

End point type	Secondary

End point timeframe:

Week 12

End point values	Ustekinumab	Ixekizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	166	136		
Units: percentage of participants				
number (not applicable)	14.5	36		

Statistical analyses

Statistical analysis title	STATISTICAL ANALYSIS 1
Comparison groups	Ustekinumab v Ixekizumab
Number of subjects included in analysis	302
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.009
Method	Regression, Logistic
Parameter estimate	Risk ratio (RR)
Point estimate	2.699
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.423
upper limit	3.975

Secondary: Percentage of Participants with a Static Physician Global Assessment (sPGA) (0,1) with at Least a 2-Point Improvement from Baseline

End point title	Percentage of Participants with a Static Physician Global Assessment (sPGA) (0,1) with at Least a 2-Point Improvement from Baseline

End point description:

The sPGA is the physician's determination of the participant's 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.

Analysis Population Description: 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 at Week 12 were considered non-responders for Non-Responder Imputation (NRI) analysis.

End point type	Secondary

End point timeframe:

Week 12

End point values	Ustekinumab	Ixekizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	166	134		
Units: percentage of participants				
number (not applicable)	57.2	83.6		

Statistical analyses

Statistical analysis title	STATISTICAL ANALYSIS 1
Comparison groups	Ustekinumab v Ixekizumab
Number of subjects included in analysis	300
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Risk ratio (RR)
Point estimate	1.469
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.244
upper limit	1.695

Secondary: Percentage of Participants with a sPGA (0) Remission

End point title	Percentage of Participants with a sPGA (0) Remission

End point description:

The sPGA is the physician's determination of the participant's 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 assessed as 0, indicates complete resolution of plaque Ps.

Analysis Population Description: All randomized participants who received at least 1 dose of study drug and had a post-baseline measurement for sPGA (0). Participants who did not meet the clinical response criteria or had missing data at Week 12 were considered non-responders for Non-Responder Imputation (NRI) analysis.

End point type	Secondary

End point timeframe:

Week 12

End point values	Ustekinumab	Ixekizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	166	136		
Units: percentage of participants				
number (not applicable)	18.1	41.9		

Statistical analyses

Statistical analysis title	STATISTICAL ANALYSIS 1
Comparison groups	Ustekinumab v Ixekizumab
Number of subjects included in analysis	302
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.021
Method	Regression, Logistic
Parameter estimate	Risk ratio (RR)
Point estimate	3.421
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.353
upper limit	5.488

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

End point title	Change from Baseline in Percent 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 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.
ANCOVA model with modified baseline observation carried forward (mBOCF) was used to produce Least Square (LS) mean with baseline, treatment group, region weight group as fixed effects.

All randomized participants who received at least 1 dose of study drug & had a baseline & post-baseline measurement for BSA affected by Ps.

mBOCF: Participants who discontinued treatment due to Adverse Event (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 12

End point values	Ustekinumab	Ixekizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	135		
Units: Percent Body Surface Affected				
least squares mean (confidence interval 95%)	-16.92 (-18.50 to -15.34)	-22.55 (-24.34 to -20.76)		

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 Ps) to 72. (the most severe disease) The PPASI was only assessed if participants have palmoplantar psoriasis at baseline.
ANCOVA model with mBOCF was used to produce LS mean with baseline, treatment group, region weight group as fixed effects.

Analysis Population Description: All randomized participants who had psoriasis in palmoplantar regions at baseline & received at least 1 dose of study drug & had baseline & post-baseline PPASI data.

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 12

End point values	Ustekinumab	Ixekizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	35		
Units: units on a scale				
least squares mean (confidence interval 95%)	-8.34 (-9.64 to -7.03)	-10.31 (-11.63 to -8.99)		

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. The composite score is derived from the sum of scores for erythema, induration, and desquamation with a scores range from 0 (none) to 4 (very severe) 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).
ANCOVA model with mBOCF was used to produce LS mean with baseline, treatment group, region weight group as fixed effects.

Analysis Population Description: All randomized participants who had psoriasis in scalp region at baseline & received at least 1 dose of study drug & had baseline & post-baseline PSSI data.

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 12

End point values	Ustekinumab	Ixekizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	119		
Units: units on a scale				
least squares mean (confidence interval 95%)	-16.00 (-17.24 to -14.77)	-19.29 (-20.67 to -17.92)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Nail Psoriasis Severity Index (NAPSI) Total Score

End point title	Change from Baseline in Nail Psoriasis Severity Index (NAPSI) Total Score

End point description:

NAPSI is a numeric, reproducible, objective tool for evaluation of fingernail(fn) Ps. This scale is used to evaluate severity of fn bed Ps & fn matrix Ps by area of involvement in the fn unit. fn is divided with imaginary horizontal & longitudinal lines into quadrants. Each fn is given a score for fn bed Ps 0(none) to 4(Ps in 4 quadrants of the fn) & fn matrix Ps 0(none) to 4(Ps in 4 quadrants in matrix), depending on presence (score of 1) or absence (score of 0) of any of the features of fn bed or matrix Ps in each quadrant.NAPSI score of a fn is sum of scores in fn bed & fn matrix from each quadrant (maximum of 8). Each fn is evaluated, then the sum of all fn equals the total NAPSI score with a range from range 0 to 80. Higher scores indicate more severe ps.
ANCOVA model with mBOCF was used to produce LS mean with baseline, treatment group, region weight group as fixed effects.

End point type	Secondary

End point timeframe:

Baseline, Week 12

Analysis Population Description: All randomized participants who had nail psoriasis at baseline & received at least 1 dose of study drug and had baseline & post-baseline NAPSI measurement.

End point values	Ustekinumab	Ixekizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	84		
Units: units on a scale				
least squares mean (confidence interval 95%)	-5.02 (-7.19 to -2.84)	-12.24 (-14.72 to -9.77)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The Itch NRS is a participant-administered, 11-point horizontal scale anchored at 0 (no itch) and 10 (worst itch imaginable). Overall severity of a participant's itching from Ps is indicated by circling the number that best describes the worst level of itching in the past 24 hours.
ANCOVA model with mBOCF was used to produce LS mean with baseline, treatment group, region weight group as fixed effects.

Analysis Population Description: All randomized participants who received at least 1 dose of study drug and had a post-baseline measurement for Itch NRS.

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 12

End point values	Ustekinumab	Ixekizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	135		
Units: units on a scale				
least squares mean (confidence interval 95%)	-4.12 (-4.51 to -3.74)	-4.56 (-4.98 to -4.14)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline on the Skin Pain Visual Analog Scale (VAS) (0,100)

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

	(VAS) (0,100)

End point description:

Skin Pain VAS is a participant administered scale designed to measure skin pain from psoriasis using a 100-millimeter (mm) horizontal VAS. Overall severity of a participant's skin pain from psoriasis at the present time is indicated by placing a single mark on the horizontal scale (0 = no skin pain; 100 = severe skin pain).
ANCOVA model with mBOCF was used to produce LS mean with baseline, treatment group, region weight group as fixed effects.

Analysis Population Description: All randomized participants who received at least 1 dose of study drug and had baseline and 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 12

End point values	Ustekinumab	Ixekizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	135		
Units: mm				
least squares mean (confidence interval 95%)	-29.92 (-32.81 to -27.04)	-33.32 (-36.44 to -30.20)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Dermatology Life Quality Index (DLQI) (0,1)

End point title	Percentage of Participants with Dermatology Life Quality Index (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). A score of 0 or 1 indicates no impact of disease on a participants quality of life.

Analysis Population Description: All randomized participants who received at least 1 dose of study drug and had a post-baseline measurement for DLQI. Participants who did not meet the clinical response criteria or had missing data at Week 12 were considered non-responders for Non-Responder Imputation (NRI) analysis.

End point type	Secondary

End point timeframe:

Week 12

End point values	Ustekinumab	Ixekizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	166	136		
Units: percentage of participants				
number (not applicable)	44.6	61.0		

Statistical analyses

Statistical analysis title	STATISTICA ANALYSIS 1
Comparison groups	Ustekinumab v Ixekizumab
Number of subjects included in analysis	302
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.012
Method	Regression, Logistic
Parameter estimate	Risk ratio (RR)
Point estimate	1.391
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.085
upper limit	1.698

Secondary: Change from Baseline on the Hospital Anxiety and Depression Scale (HADS) Depression Subscale

End point title	Change from Baseline on the Hospital Anxiety and Depression Scale (HADS) Depression Subscale

End point description:

The HADS is a participant-rated instrument used to assess both anxiety and depression. This instrument consists of 14 items questionnaire, each item is rated on a 4-point scale, giving maximum scores of 21 for anxiety and depression. Scores of 11 or more on either subscale are considered to be a significant 'case' of psychological morbidity, while scores of 8-10 represent 'borderline' and 0-7, 'normal.
ANCOVA model with mBOCF was used to produce LS mean with baseline, treatment group, region weight group as fixed effects.

Analysis Population Description: All randomized participants who received at least 1 dose of study drug and had baseline and post-baseline measurement for HADS depression subscale.

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 12

End point values	Ustekinumab	Ixekizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162	134		
Units: units on a scale				
least squares mean (confidence interval 95%)	-0.96 (-1.38 to -0.54)	-1.20 (-1.65 to -0.74)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline on the Hospital Anxiety and Depression Scale (HADS) Anxiety Subscale.

End point title	Change from Baseline on the Hospital Anxiety and Depression Scale (HADS) Anxiety Subscale.

End point description:

The HADS is a participant-rated instrument used to assess both anxiety and depression. This instrument consists of 14 items questionnaire, each item is rated on a 4-point scale, giving maximum scores of 21 for anxiety and depression. Scores of 11 or more on either subscale are considered to be a significant 'case' of psychological morbidity, while scores of 8-10 represent 'borderline' and 0-7, 'normal.
ANCOVA model with mBOCF was used to produce LS mean with baseline, treatment group, region weight group as fixed effects.

Analysis Population Description: All randomized participants who received at least 1 dose of study drug and had baseline and a post-baseline measurement for HADS anxiety subscale.

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 12

End point values	Ustekinumab	Ixekizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162	134		
Units: units on a scale				
least squares mean (confidence interval 95%)	-0.90 (-1.37 to -0.43)	-1.27 (-1.80 to -0.73)		

Statistical analyses

No statistical analyses for this end point

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

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

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. Items from 8 domains contribute to the PCS. The summary scores range from 0 to 100, with higher scores indicating better levels of function and/or better health. SF-36 acute version was used, which has a 1 week recall period.
ANCOVA model with mBOCF was used to produce LS mean with baseline, treatment group, region weight group as fixed effects.

Analysis Population Description: All randomized participants who received at least 1 dose of study drug and had baseline and post-baseline measurement for SF-36 PCS score.

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

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Ustekinumab	Ixekizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	133		
Units: units on a scale				
least squares mean (confidence interval 95%)	3.10 (1.97 to 4.23)	5.03 (3.80 to 6.26)		

Statistical analyses

No statistical analyses for this end point

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

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

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. Items from 8 domains contribute to the PCS. The summary scores range from 0 to 100, with higher scores indicating better levels of function and/or better health. SF-36 acute version was used, which has a 1 week recall period.
ANCOVA model with mBOCF was used to produce LS mean with baseline, treatment group, region weight group as fixed effects.

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

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Ustekinumab	Ixekizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	133		
Units: units on a scale				
least squares mean (confidence interval 95%)	2.36 (0.87 to 3.86)	2.96 (1.33 to 4.59)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The Patient Global Assessment of Disease Severity is a single-item participant-reported outcome measure on which participants are asked to rate the severity of their psoriasis "today" from 0 (Clear) = no psoriasis, to 5 (Severe) = the worst their psoriasis has ever been.
ANCOVA model with mBOCF was used to produce LS mean with baseline, treatment group, region weight group as fixed effects.

Analysis Population Description: All randomized participants who received at least 1 dose of study drug and had baseline and 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 12

End point values	Ustekinumab	Ixekizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	135		
Units: units on a scale				
least squares mean (confidence interval 95%)	-2.60 (-2.78 to -2.42)	-3.07 (-3.26 to -2.88)		

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

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

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).
ANCOVA model was used to produce LS mean with baseline, treatment group, region weight group as fixed effects.

Analysis Population Description: All randomized participants who received at least 1 dose of study drug and had baseline and post-baseline measurement for EQ-5D 5L "Bolt On" PSO-Index.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Ustekinumab	Ixekizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	134		
Units: units on a scale				
least squares mean (confidence interval 95%)	0.11 (0.09 to 0.13)	0.15 (0.13 to 0.17)		

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) VAS

End point title	Change from Baseline in European Quality of Life - 5 Dimensions 5 Level (EQ-5D 5L) VAS

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). ANCOVA model with mBOCF was used to produce LS mean with baseline, treatment group, region weight group as fixed effects.

Analysis population Description: All randomized participants who received at least 1 dose of study drug and had baseline and post-baseline measurement for EQ-5D 5L 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 12

End point values	Ustekinumab	Ixekizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	134		
Units: mm				
least squares mean (confidence interval 95%)	8.75 (5.77 to 11.74)	12.24 (9.01 to 15.46)		

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) United Kingdom(UK) population-based index score

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

End point description:

The EQ-5D-5L descriptive system comprises 5 dimensions, each with 5 levels. The EQ-5D-5L health states were converted into a single summary index by applying a crosswalk using a UK Population value set to each of the levels in each dimension. This produced patient-level index scores between -0.594 and 1.0 (worse to better health).
ANCOVA model with mBOCF was used to produce LS mean with baseline, treatment group, region weight group as fixed effects.

Analysis Population Description: All randomized participants who received at least 1 dose of study drug & had baseline & post-baseline EQ-5D 5L UK population-based index score measurement.

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 12

End point values	Ustekinumab	Ixekizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	134		
Units: units on a scale				
least squares mean (confidence interval 95%)	0.12 (0.09 to 0.15)	0.15 (0.12 to 0.18)		

Statistical analyses

No statistical analyses for this end point

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

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

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 & WPAI-PSO absenteeism score is derived from these questions. Each WPAI score is expressed as an impairment percentage (0-100), with higher scores representing greater impairment (worse outcomes).
ANCOVA model with mBOCF was used to produce LS mean with baseline, treatment group, region weight group as fixed effects.

Analysis Population Description: 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 12

End point values	Ustekinumab	Ixekizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	87		
Units: units on a scale				
least squares mean (confidence interval 95%)	-1.42 (-4.55 to 1.72)	-0.46 (-3.51 to 2.60)		

Statistical analyses

No statistical analyses for this end point

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

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

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 & WPAI-PSO Presenteeism score is derived from these questions. each WPAI score is expressed as an impairment percentage (0-100), with higher scores representing greater impairment (worse outcomes).
ANCOVA model with mBOCF was used to produce LS mean with baseline, treatment group, region weight group as fixed effects.

Analysis Population Description: All randomized participants who received at least 1 dose of study drug and had baseline and post-baseline measurement for WPAI-PSO presenteeism score.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Ustekinumab	Ixekizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	92		
Units: units on a scale				
least squares mean (confidence interval 95%)	-15.53 (-18.33 to -12.72)	-16.91 (-19.71 to -14.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline on the Work Productivity Activity Impairment Questionnaire-Psoriasis (WPAI-PSO) work impairment score.

End point title	Change From Baseline on the Work Productivity Activity Impairment Questionnaire-Psoriasis (WPAI-PSO) 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 & WPAI-PSO work impairment score is derived from these questions. each WPAI score is expressed as an impairment percentage (0-100), with higher scores representing greater impairment (worse outcomes).
ANCOVA model with mBOCF was used to produce LS mean with baseline, treatment group, region weight group as fixed effects.

Analysis Population Description: All randomized participants who received at least 1 dose of study drug and had baseline and post-baseline measurement for WPAI-PSO work impairment score.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Ustekinumab	Ixekizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	87		
Units: units on a scale				
least squares mean (confidence interval 95%)	-15.05 (-19.25 to -10.85)	-16.27 (-20.39 to -12.16)		

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 & WPAI-PSO impairment in activities performed outside of work score is derived from these questions. each WPAI score is expressed as an impairment percentage (0-100), with higher scores representing greater impairment (worse outcomes).
ANCOVA model with mBOCF was used to produce LS mean with baseline, treatment group, region weight group as fixed effects.

Analysis Population Description: All randomized participants who received at least 1 dose of study drug & had baseline & post-baseline data for WPAI-PSO impairment in activities performed outside work.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Ustekinumab	Ixekizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	127		
Units: units on a scale				
least squares mean (confidence interval 95%)	-19.14 (-21.79 to -16.48)	-23.06 (-26.04 to -20.09)		

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	Ustekinumab - Induction period

Reporting group description:

45 milligram (mg) Ustekinumab given as subcutaneous (SC) injection for participants ≤100 kilograms (kg) and 90 mg SC injection for participants >100 kg. Placebo for Ixekizumab injection was used for blinding.

Reporting group title	Ixekizumab - Induction period

Reporting group description:

160 mg Ixekizumab given as two subcutaneous (SC) injections at baseline followed by 80 mg Ixekizumab given as a single SC injection once every 2 weeks. Placebo for Ustekinumab injection was used for blinding.

Reporting group title	Ustekinumab - Maintenance period

Reporting group description:

45 milligram (mg) Ustekinumab given as Subcutaneous (SC) injection for participants ≤100 kilograms (kg) and 90 mg SC injection for participants >100 kg. Placebo for Ixekizumab injection was used for blinding.

Reporting group title	Ixekizumab - Maintenance period

Reporting group description:

80 mg Ixekizumab given as a single SC injection once every 4 weeks. Placebo for Ustekinumab injection was used for blinding.

Reporting group title	Ixekizumab/Ustekinumab - Post Treatment Follow-up

Reporting group description:

Participants were allowed to continue the treatment administered during the blinded period or any other psoriasis treatment.

Serious adverse events	Ustekinumab - Induction period	Ixekizumab - Induction period	Ustekinumab - Maintenance period
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 166 (0.00%)	2 / 135 (1.48%)	6 / 164 (3.66%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
ankle fracture			
alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	0 / 166 (0.00%)	0 / 135 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
angina unstable			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 166 (0.00%)	1 / 135 (0.74%)	0 / 164 (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
myocardial infarction			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 166 (0.00%)	0 / 135 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
rectal haemorrhage			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 166 (0.00%)	0 / 135 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
cholecystitis acute			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 166 (0.00%)	0 / 135 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cholelithiasis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 166 (0.00%)	0 / 135 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
chronic obstructive pulmonary disease			

alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 166 (0.00%)	0 / 135 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
eczema			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 166 (0.00%)	0 / 135 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
depression			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 166 (0.00%)	0 / 135 (0.00%)	0 / 164 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
arthritis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 166 (0.00%)	0 / 135 (0.00%)	0 / 164 (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
pseudarthrosis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 166 (0.00%)	0 / 135 (0.00%)	0 / 164 (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
psoriatic arthropathy			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 166 (0.00%)	0 / 135 (0.00%)	0 / 164 (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
rotator cuff syndrome			

alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 166 (0.00%)	0 / 135 (0.00%)	0 / 164 (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 / 166 (0.00%)	0 / 135 (0.00%)	0 / 164 (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 bacterial			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 166 (0.00%)	1 / 135 (0.74%)	0 / 164 (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
Metabolism and nutrition disorders			
obesity			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 166 (0.00%)	0 / 135 (0.00%)	1 / 164 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Ixekizumab - Maintenance period	Ixekizumab/Ustekinumab - Post Treatment Follow-up	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 131 (5.34%)	2 / 217 (0.92%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
ankle fracture			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 131 (0.00%)	0 / 217 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			

angina unstable			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 131 (0.00%)	0 / 217 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
myocardial infarction			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 131 (0.00%)	0 / 217 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
rectal haemorrhage			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 131 (0.76%)	0 / 217 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
cholecystitis acute			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 131 (0.00%)	0 / 217 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
cholelithiasis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 131 (0.76%)	0 / 217 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
chronic obstructive pulmonary disease			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 131 (0.00%)	0 / 217 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Skin and subcutaneous tissue disorders			
eczema			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 131 (0.76%)	0 / 217 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
depression			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 131 (0.76%)	0 / 217 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
arthritis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 131 (0.76%)	0 / 217 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pseudarthrosis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 131 (0.76%)	0 / 217 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
psoriatic arthropathy			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 131 (0.00%)	1 / 217 (0.46%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
rotator cuff syndrome			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	1 / 131 (0.76%)	0 / 217 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

erysipelas			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 131 (0.00%)	1 / 217 (0.46%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastroenteritis bacterial			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 131 (0.00%)	0 / 217 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
obesity			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	0 / 131 (0.00%)	0 / 217 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Ustekinumab - Induction period	Ixekizumab - Induction period	Ustekinumab - Maintenance period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	55 / 166 (33.13%)	40 / 135 (29.63%)	65 / 164 (39.63%)
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	4 / 166 (2.41%)	2 / 135 (1.48%)	11 / 164 (6.71%)
occurrences (all)	4	2	11
Nervous system disorders			
headache			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	12 / 166 (7.23%)	7 / 135 (5.19%)	12 / 164 (7.32%)
occurrences (all)	17	9	19
General disorders and administration site conditions			

injection site erythema alternative dictionary used: MedDRA 19.1 subjects affected / exposed occurrences (all)	0 / 166 (0.00%) 0	10 / 135 (7.41%) 15	0 / 164 (0.00%) 0
Musculoskeletal and connective tissue disorders arthralgia alternative dictionary used: MedDRA 19.1 subjects affected / exposed occurrences (all)	8 / 166 (4.82%) 8	3 / 135 (2.22%) 3	11 / 164 (6.71%) 16
back pain alternative dictionary used: MedDRA 19.1 subjects affected / exposed occurrences (all)	4 / 166 (2.41%) 5	2 / 135 (1.48%) 2	9 / 164 (5.49%) 11
Infections and infestations nasopharyngitis alternative dictionary used: MedDRA 19.1 subjects affected / exposed occurrences (all)	34 / 166 (20.48%) 39	23 / 135 (17.04%) 27	40 / 164 (24.39%) 52

Non-serious adverse events	Ixekizumab - Maintenance period	Ixekizumab/Ustekinumab - Post Treatment Follow-up	
Total subjects affected by non-serious adverse events subjects affected / exposed	50 / 131 (38.17%)	0 / 217 (0.00%)	
Vascular disorders hypertension alternative dictionary used: MedDRA 19.1 subjects affected / exposed occurrences (all)	4 / 131 (3.05%) 5	0 / 217 (0.00%) 0	
Nervous system disorders headache alternative dictionary used: MedDRA 19.1 subjects affected / exposed occurrences (all)	10 / 131 (7.63%) 17	0 / 217 (0.00%) 0	
General disorders and administration site conditions injection site erythema alternative dictionary used: MedDRA 19.1			

subjects affected / exposed	2 / 131 (1.53%)	0 / 217 (0.00%)	
occurrences (all)	4	0	
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	8 / 131 (6.11%)	0 / 217 (0.00%)	
occurrences (all)	8	0	
back pain			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	5 / 131 (3.82%)	0 / 217 (0.00%)	
occurrences (all)	5	0	
Infections and infestations			
nasopharyngitis			
alternative dictionary used: MedDRA 19.1			
subjects affected / exposed	36 / 131 (27.48%)	0 / 217 (0.00%)	
occurrences (all)	47	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 February 2016	Reworded the note on one of the exclusion criterion. Modified one of the exclusion criterion. Clarified the unblinding process. Clarified key secondary analysis for sPGA. Corrected the Study Schedule. Clarification of the testing parameters of the hepatitis B monitoring. Recalculated blood volumes to remove retest sample collections. immunogenicity blood sample collection was added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported