Clinical trial results:
A Phase 3, Multicenter, Randomized, Double-blind Study to Evaluate the Efficacy and Safety of Guselkumab for the Treatment of Subjects With Moderate to Severe Plaque-type Psoriasis and an Inadequate Response to Ustekinumab

Summary

EudraCT number	2014-000721-20
Trial protocol	GB ES
Global end of trial date	24 May 2016

Results information

Result version number	v1 (current)
This version publication date	27 May 2017
First version publication date	27 May 2017

Trial information

Trial identification

Sponsor protocol code	CNTO1959PSO3003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02203032
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, LLC
Sponsor organisation address	920 Route, 202 Raritan, New Jersey , United States, 08869
Public contact	Clinical Registry group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com

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	24 May 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 May 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objectives of this study were to compare the efficacy of the following 2 treatment groups in subjects who had an inadequate (Investigator's Global Assessment [IGA] >= 2) response to ustekinumab at Week 16: 1) switching to guselkumab treatment, or 2) remaining on ustekinumab treatment, and to assess the safety and tolerability of guselkumab in subjects with moderate to severe plaque-type psoriasis and an inadequate (IGA>=2) response to ustekinumab at Week 16.

Protection of trial subjects:

The safety and tolerability of guselkumab and ustekinumab were monitored by collecting information on adverse events (AEs), including injection-site reactions (ISRs), allergic reactions, clinical laboratory tests, physical examinations, vital signs, concomitant medication review, and early detection of active tuberculosis (TB). An independent data monitoring committee was commissioned for this study to review unblinded data at regularly scheduled intervals.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 October 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 19
Country: Number of subjects enrolled	Canada: 61
Country: Number of subjects enrolled	Germany: 96
Country: Number of subjects enrolled	Spain: 24
Country: Number of subjects enrolled	United Kingdom: 11
Country: Number of subjects enrolled	Korea, Republic of: 29
Country: Number of subjects enrolled	Poland: 294
Country: Number of subjects enrolled	Russian Federation: 88
Country: Number of subjects enrolled	Taiwan: 55
Country: Number of subjects enrolled	United States: 194
Worldwide total number of subjects	871
EEA total number of subjects	425

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)	818
From 65 to 84 years	53
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 1105 subjects were screened for this study. Among them 871 subjects were enrolled and received study treatment. The target population was adult men or women with a diagnosis of plaque-type psoriasis (with or without psoriatic arthritis) for at least 6 months before the first administration of study drug.

Period 1

Period 1 title	Week 0 - Week 16 (Open Label Run-in)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Ustekinumab

Arm description:

Subject received ustekinumab 45 milligram (mg) (subjects weighing less than or equal to [<=]100 kilogram [kg]) or 90 mg (subjects weighing >100 kg) at Week 0 and 4.

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

Dosage and administration details:

Enrolled subjects received ustekinumab 45 mg or 90 mg at Weeks 0 and 4 [according to their weight at baseline (Week 0)].

Number of subjects in period 1	Ustekinumab
Started	871
Completed	853
Not completed	18
Consent withdrawn by subject	6
Adverse event, non-fatal	1
Other	2
Adverse event, serious non-fatal	1
Lost to follow-up	3
Lack of efficacy	1
Protocol deviation	4

Period 2

Period 2 title	Blinded Phase (Week 16 - Week 44)
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	Guselkumab (Randomized)

Arm description:

Subjects with an IGA>=2 at Week 16 were randomized to guselkumab, received guselkumab 100 mg at Weeks 16, 20, 28, 36, and 44 and placebo for ustekinumab at Weeks 16, 28, and 40.

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

Dosage and administration details:

Subjects received guselkumab 100 mg at Weeks 16, 20, 28, 36 and 44

Investigational medicinal product name	Placebo for Ustekinumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects randomized to guselkumab received placebo for ustekinumab at Weeks 16, 28, and 40.

Arm title	Ustekinumab (Randomized)

Arm description:

Subjects with an IGA>=2 at Week 16 were randomized to ustekinumab, continued to receive ustekinumab, according to their baseline (Week 0) weight, at Weeks 16, 28, and 40, and placebo for guselkumab at Weeks 16, 20, 28, 36, and 44.

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

Dosage and administration details:

Subjects randomized to ustekinumab continued to receive ustekinumab, according to their baseline (Week 0) weight, at Weeks 16, 28, and 40.

Investigational medicinal product name	Placebo for Guselkumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects randomized to ustekinumab received placebo for guselkumab at Weeks 16, 20, 28, 36, and 44.

Arm title	Ustekinumab (Non randomized Open Label (OL) Continuation)

Arm description:

Subjects with an IGA=0 or 1 at Week 16 received ustekinumab 45 mg or 90 mg (according to their baseline weight [Week 0]) at Weeks 16, 28, and 40.

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

Dosage and administration details:

Subjects received ustekinumab (according to their baseline weight [Week 0]) at Weeks 16, 28, and 40.

Number of subjects in period 2	Guselkumab (Randomized)	Ustekinumab (Randomized)	Ustekinumab (Non randomized Open Label (OL) Continuation)
Started	135	133	585
Completed	126	113	568
Not completed	9	20	17
Adverse event, serious fatal	-	-	1
Consent withdrawn by subject	2	5	5
Adverse event, non-fatal	1	2	3
Other	1	2	3
Adverse event, serious non-fatal	2	-	3
Lost to follow-up	-	1	1
Lack of efficacy	3	10	1

Baseline characteristics

Reporting groups	
Reporting group title	Ustekinumab
Reporting group description:	
Subject received ustekinumab 45 milligram (mg) (subjects weighing less than or equal to [<=]100 kilogram [kg]) or 90 mg (subjects weighing >100 kg) at Week 0 and 4.	

Reporting group values	Ustekinumab	Total	
Number of subjects	871	871	
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	818	818	
From 65 to 84 years	53	53	
85 years and over	0	0	
Title for AgeContinuous Units: years			
arithmetic mean	43.1		
standard deviation	± 13.21	-	
Title for Gender Units: subjects			
Female	305	305	
Male	566	566	

End points

End points reporting groups

Reporting group title	Ustekinumab
Reporting group description:	
Subject received ustekinumab 45 milligram (mg) (subjects weighing less than or equal to [<=]100 kilogram [kg]) or 90 mg (subjects weighing >100 kg) at Week 0 and 4.	
Reporting group title	Guselkumab (Randomized)
Reporting group description:	
Subjects with an IGA>=2 at Week 16 were randomized to guselkumab, received guselkumab 100 mg at Weeks 16, 20, 28, 36, and 44 and placebo for ustekinumab at Weeks 16, 28, and 40.	
Reporting group title	Ustekinumab (Randomized)
Reporting group description:	
Subjects with an IGA>=2 at Week 16 were randomized to ustekinumab, continued to receive ustekinumab, according to their baseline (Week 0) weight, at Weeks 16, 28, and 40, and placebo for guselkumab at Weeks 16, 20, 28, 36, and 44.	
Reporting group title	Ustekinumab (Non randomized Open Label (OL) Continuation)
Reporting group description:	
Subjects with an IGA=0 or 1 at Week 16 received ustekinumab 45 mg or 90 mg (according to their baseline weight [Week 0]) at Weeks 16, 28, and 40.	

Primary: Number of Visits at Which Subjects Achieved an Investigator's Global Assessment (IGA) Response of Cleared (0) or Minimal (1) and at Least a 2 Grade Improvement (from Week 16) Between Week 28 and Week 40

End point title	Number of Visits at Which Subjects Achieved an Investigator's Global Assessment (IGA) Response of Cleared (0) or Minimal (1) and at Least a 2 Grade Improvement (from Week 16) Between Week 28 and Week 40
End point description:	
The IGA documents the investigator's assessment of the subjects psoriasis at a given time point. Overall lesions are graded for induration, erythema, and scaling on a scale of 0 to 4 (higher score = more severe). The subjects psoriasis was assessed as cleared (0), minimal (1), mild (2), moderate (3), or severe (4). The efficacy population included all subjects who were randomized at Week 16 (randomized analysis set).	
End point type	Primary
End point timeframe:	
Week 28 through Week 40	

End point values	Guselkumab (Randomized)	Ustekinumab (Randomized)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	133		
Units: visits				
arithmetic mean (standard deviation)	1.5 (± 1.57)	0.7 (± 1.26)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Guselkumab (Randomized) v Ustekinumab (Randomized)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Row mean score test

Secondary: Number of Visits at Which Subjects Achieved a Psoriasis Area and Severity Index (PASI) 90 Response Between Week 28 and Week 40

End point title	Number of Visits at Which Subjects Achieved a Psoriasis Area and Severity Index (PASI) 90 Response Between Week 28 and Week 40

End point description:

The PASI is a system used for assessing and grading the severity of psoriatic lesions. In the PASI system, the body is divided into 4 regions: the head, trunk, upper extremities, and lower extremities. Each of these areas were assessed separately for the percentage of the area involved, which translates to a numeric score that ranges from 0 to 6, and for erythema, induration, and scaling, which are each rated on a scale of 0 to 4. The PASI produces a numeric score that can range from 0 to 72. A higher score indicates more severe disease. A PASI 90 response represents subjects achieved at least a 90 percent improvement from baseline in the PASI score. The efficacy population included all subjects who were randomized at Week 16 (randomized analysis set).

End point type	Secondary

End point timeframe:

Week 28 through Week 40

End point values	Guselkumab (Randomized)	Ustekinumab (Randomized)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	133		
Units: visits				
arithmetic mean (standard deviation)	2.2 (± 1.69)	1.1 (± 1.53)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Guselkumab (Randomized) v Ustekinumab (Randomized)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Row mean score test

Secondary: Number of Visits at Which Subjects Achieved an IGA Score of Cleared

(0) Between Week 28 and Week 40

End point title	Number of Visits at Which Subjects Achieved an IGA Score of Cleared (0) Between Week 28 and Week 40

End point description:

The IGA documents the investigator's assessment of the subjects psoriasis at a given time point. Overall lesions are graded for induration, erythema, and scaling on a scale of 0 to 4 (higher score = more severe). The subjects psoriasis is assessed as cleared (0), minimal (1), mild (2), moderate (3), or severe (4). The efficacy population included all subjects who were randomized at Week 16 (randomized analysis set).

End point type	Secondary

End point timeframe:

Week 28 through Week 40

End point values	Guselkumab (Randomized)	Ustekinumab (Randomized)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	133		
Units: visits				
arithmetic mean (standard deviation)	0.9 (± 1.34)	0.4 (± 1.06)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Guselkumab (Randomized) v Ustekinumab (Randomized)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Row mean score test

Secondary: Percentage of Subjects With an Investigator’s Global Assessment (IGA) Score of Cleared (0) or Minimal (1) and at Least a 2 Grade Improvement (From Week 16) at Week 28

End point title	Percentage of Subjects With an Investigator’s Global Assessment (IGA) Score of Cleared (0) or Minimal (1) and at Least a 2 Grade Improvement (From Week 16) at Week 28

End point description:

The IGA documents the investigator's assessment of the subjects psoriasis at a given time point. Overall lesions are graded for induration, erythema, and scaling on a scale of 0 to 4 (higher score = more severe). The subjects psoriasis is assessed as cleared (0), minimal (1), mild (2), moderate (3), or severe (4). The efficacy population included all subjects who were randomized at Week 16 (randomized analysis set).

End point type	Secondary

End point timeframe:

Week 28

End point values	Guselkumab (Randomized)	Ustekinumab (Randomized)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	133		
Units: percentage of subjects				
number (not applicable)	31.1	14.3		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Guselkumab (Randomized) v Ustekinumab (Randomized)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Cochran-Mantel-Haenszel

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to Week 60	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups	
Reporting group title	Ustekinumab Open Label Run-in (Week 0 - Week 16)
Reporting group description: Subject received ustekinumab 45 milli gram (mg) (subjects weighing less than or equal to [<=]100 kilogram [kg]) and 90 mg (Subjects weighing >100 kg) at Week 0 and 4.	
Reporting group title	Guselkumab Randomized (Week 16 - Week 60)
Reporting group description: Subjects (with an IGA>=2 at Week 16) received guselkumab 100 mg at Weeks 16, 20, 28, 36, and 44 and placebo for ustekinumab at Weeks 16, 28, and 40.	
Reporting group title	Ustekinumab Randomized (Week 16 - Week 60)
Reporting group description: Subjects (with an IGA>=2 at Week 16) received ustekinumab, according to their weight at baseline (Week 0), at Weeks 16, 28, and 40, and placebo for guselkumab at Weeks 16, 20, 28, 36, and 44.	
Reporting group title	Ustekinumab Nonrandomized OL Continuation (Week 16 - Week 60)
Reporting group description: Subjects (with an IGA=0 or 1) at Week 16 received ustekinumab (according to their baseline weight [Week 0]) at Weeks 16, 28, and 40.	

Serious adverse events	Ustekinumab Open Label Run-in (Week 0 - Week 16)	Guselkumab Randomized (Week 16 - Week 60)	Ustekinumab Randomized (Week 16 - Week 60)
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 871 (1.26%)	9 / 135 (6.67%)	6 / 133 (4.51%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bile Duct Cancer			
subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	0 / 133 (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 Carcinoma Metastatic			
subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	0 / 133 (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

Squamous Cell Carcinoma			
subjects affected / exposed	0 / 871 (0.00%)	1 / 135 (0.74%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional Cell Carcinoma			
subjects affected / exposed	0 / 871 (0.00%)	1 / 135 (0.74%)	0 / 133 (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
Pregnancy, puerperium and perinatal conditions			
Abortion Spontaneous			
subjects affected / exposed	0 / 871 (0.00%)	1 / 135 (0.74%)	0 / 133 (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
Ectopic Pregnancy			
subjects affected / exposed	0 / 871 (0.00%)	1 / 135 (0.74%)	0 / 133 (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
General disorders and administration site conditions			
Chest Discomfort			
subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	0 / 133 (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
Chest Pain			
subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Alcohol Poisoning			
subjects affected / exposed	1 / 871 (0.11%)	0 / 135 (0.00%)	0 / 133 (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
Contusion			

subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	0 / 133 (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
Scapula Fracture			
subjects affected / exposed	1 / 871 (0.11%)	0 / 135 (0.00%)	0 / 133 (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
Toxicity to Various Agents			
subjects affected / exposed	0 / 871 (0.00%)	1 / 135 (0.74%)	0 / 133 (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
Tibia Fracture			
subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute Myocardial Infarction			
subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	1 / 133 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina Unstable			
subjects affected / exposed	0 / 871 (0.00%)	1 / 135 (0.74%)	0 / 133 (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
Atrial Fibrillation			
subjects affected / exposed	1 / 871 (0.11%)	0 / 135 (0.00%)	0 / 133 (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
Myocardial Infarction			
subjects affected / exposed	0 / 871 (0.00%)	2 / 135 (1.48%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus Node Dysfunction			

subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	0 / 133 (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			
Migraine			
subjects affected / exposed	0 / 871 (0.00%)	1 / 135 (0.74%)	0 / 133 (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
Syncope			
subjects affected / exposed	1 / 871 (0.11%)	0 / 135 (0.00%)	0 / 133 (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
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	0 / 133 (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
Eye disorders			
Blindness			
subjects affected / exposed	1 / 871 (0.11%)	0 / 135 (0.00%)	0 / 133 (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
Cataract			
subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	0 / 133 (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
Retinal Artery Embolism			
subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	0 / 133 (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
Retinal Detachment			
subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	1 / 133 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	0 / 133 (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			
subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large Intestinal Stenosis			
subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	0 / 133 (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			
Bile Duct Stenosis			
subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	0 / 133 (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
Cholecystitis			
subjects affected / exposed	1 / 871 (0.11%)	0 / 135 (0.00%)	0 / 133 (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
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	1 / 133 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoriasis			
subjects affected / exposed	2 / 871 (0.23%)	0 / 135 (0.00%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back Pain			

subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	1 / 133 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot Deformity			
subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	0 / 133 (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			
Anal Abscess			
subjects affected / exposed	1 / 871 (0.11%)	0 / 135 (0.00%)	0 / 133 (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
Arthritis Bacterial			
subjects affected / exposed	0 / 871 (0.00%)	1 / 135 (0.74%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	0 / 133 (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
Diverticulitis			
subjects affected / exposed	1 / 871 (0.11%)	0 / 135 (0.00%)	0 / 133 (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
Epididymitis			
subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	0 / 133 (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
Paraspinal Abscess			
subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	0 / 133 (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
Periodontitis			

subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia Bacterial			
subjects affected / exposed	1 / 871 (0.11%)	0 / 135 (0.00%)	0 / 133 (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
Salpingitis			
subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes Mellitus			
subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	1 / 133 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 2 Diabetes Mellitus			
subjects affected / exposed	0 / 871 (0.00%)	0 / 135 (0.00%)	1 / 133 (0.75%)
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	Ustekinumab Nonrandomized OL Continuation (Week 16 - Week 60)		
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 585 (3.42%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bile Duct Cancer			
subjects affected / exposed	1 / 585 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatic Carcinoma Metastatic			

subjects affected / exposed	1 / 585 (0.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Squamous Cell Carcinoma			
subjects affected / exposed	0 / 585 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transitional Cell Carcinoma			
subjects affected / exposed	0 / 585 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion Spontaneous			
subjects affected / exposed	0 / 585 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ectopic Pregnancy			
subjects affected / exposed	0 / 585 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest Discomfort			
subjects affected / exposed	1 / 585 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chest Pain			
subjects affected / exposed	1 / 585 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Alcohol Poisoning			

subjects affected / exposed	0 / 585 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Contusion				
subjects affected / exposed	1 / 585 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Scapula Fracture				
subjects affected / exposed	0 / 585 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Toxicity to Various Agents				
subjects affected / exposed	0 / 585 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tibia Fracture				
subjects affected / exposed	1 / 585 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute Myocardial Infarction				
subjects affected / exposed	1 / 585 (0.17%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Angina Unstable				
subjects affected / exposed	0 / 585 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial Fibrillation				
subjects affected / exposed	0 / 585 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial Infarction				

subjects affected / exposed	0 / 585 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sinus Node Dysfunction			
subjects affected / exposed	1 / 585 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Migraine			
subjects affected / exposed	0 / 585 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 585 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 585 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Blindness			
subjects affected / exposed	0 / 585 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cataract			
subjects affected / exposed	2 / 585 (0.34%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Retinal Artery Embolism			
subjects affected / exposed	1 / 585 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Retinal Detachment				
subjects affected / exposed	0 / 585 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Constipation				
subjects affected / exposed	1 / 585 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	1 / 585 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Large Intestinal Stenosis				
subjects affected / exposed	1 / 585 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Bile Duct Stenosis				
subjects affected / exposed	1 / 585 (0.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholecystitis				
subjects affected / exposed	0 / 585 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Eczema				
subjects affected / exposed	0 / 585 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psoriasis				

subjects affected / exposed	0 / 585 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	0 / 585 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Foot Deformity			
subjects affected / exposed	1 / 585 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Anal Abscess			
subjects affected / exposed	0 / 585 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arthritis Bacterial			
subjects affected / exposed	0 / 585 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	1 / 585 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	0 / 585 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Epididymitis			
subjects affected / exposed	1 / 585 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Paraspinal Abscess			
subjects affected / exposed	1 / 585 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Periodontitis			
subjects affected / exposed	1 / 585 (0.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia Bacterial			
subjects affected / exposed	0 / 585 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Salpingitis			
subjects affected / exposed	1 / 585 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetes Mellitus			
subjects affected / exposed	0 / 585 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Type 2 Diabetes Mellitus			
subjects affected / exposed	0 / 585 (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	Ustekinumab Open Label Run-in (Week 0 - Week 16)	Guselkumab Randomized (Week 16 - Week 60)	Ustekinumab Randomized (Week 16 - Week 60)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	80 / 871 (9.18%)	37 / 135 (27.41%)	33 / 133 (24.81%)
Infections and infestations			
Nasopharyngitis			

subjects affected / exposed	47 / 871 (5.40%)	23 / 135 (17.04%)	23 / 133 (17.29%)
occurrences (all)	47	23	23
Upper Respiratory Tract Infection			
subjects affected / exposed	33 / 871 (3.79%)	15 / 135 (11.11%)	11 / 133 (8.27%)
occurrences (all)	33	15	11

Non-serious adverse events	Ustekinumab Nonrandomized OL Continuation (Week 16 - Week 60)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	60 / 585 (10.26%)		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	33 / 585 (5.64%)		
occurrences (all)	33		
Upper Respiratory Tract Infection			
subjects affected / exposed	27 / 585 (4.62%)		
occurrences (all)	27		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 July 2014	Electrocardiogram (ECG) collection timepoints were added beyond Week 0 (Weeks 16, 32, and 52) to obtain additional ECG measurements for safety assessment in randomized subjects only; A physical examination and a urine pregnancy test were added at Week 52; An additional discontinuation criterion was added for subjects who experience signs and symptoms suspicious for reversible posterior leukoencephalopathy syndrome; Information was added about the presence of dry natural rubber on the ustekinumab prefilled syringe (PFS) needle cover, which might cause allergic reactions in individuals sensitive to latex.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported