Clinical trial results:
Phase 3b, Multicenter, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of Guselkumab Administered Subcutaneously in Participants with Active Psoriatic Arthritis and an Inadequate Response to Anti-Tumor Necrosis Factor Alpha (Anti-TNF) Therapy COSMOS

Summary

EudraCT number	2018-003214-41
Trial protocol	BE FR GB ES PL PT HU BG GR IT
Global end of trial date	11 November 2020

Results information

Result version number	v1 (current)
This version publication date	17 November 2021
First version publication date	17 November 2021

Trial information

Trial identification

Sponsor protocol code	CNTO1959PSA3003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03796858
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research and Development, LLC
Sponsor organisation address	920, US Highway, Route 202, South Raritan, United States, 08869
Public contact	Janssen Research and Development, LLC, Clinical Registry Group, ClinicalTrialsEU@its.jnj.com
Scientific contact	Janssen Research and Development, LLC, Clinical Registry Group, 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	11 November 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate guselkumab efficacy versus placebo in subjects with active Psoriatic Arthritis (PsA) and an inadequate response to anti-tumor necrosis factor alpha (anti-TNF alpha) therapy by assessing the reduction in signs and symptoms of joint and skin disease.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements. The safety evaluations included monitoring of adverse events, serious adverse events (SAEs), injection site and allergic reactions, clinical laboratory parameters (hematology and chemistry; urine pregnancy test), electronic Columbia-Suicide Severity Rating Scale (eC-SSRS), physical examinations, vital signs and electrocardiogram (ECG; Week 0 only).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 March 2019
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	Belgium: 1
Country: Number of subjects enrolled	Bulgaria: 24
Country: Number of subjects enrolled	Germany: 16
Country: Number of subjects enrolled	Spain: 16
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	Hungary: 15
Country: Number of subjects enrolled	Israel: 7
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Poland: 19
Country: Number of subjects enrolled	Portugal: 1
Country: Number of subjects enrolled	Russian Federation: 95
Country: Number of subjects enrolled	Ukraine: 74
Worldwide total number of subjects	285
EEA total number of subjects	101

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)	258
From 65 to 84 years	27
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 285 subjects were randomized to receive study intervention;189 subjects were randomized to the guselkumab treatment group and 96 subjects were randomized to the placebo treatment group.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: Guselkumab 100 mg q8w

Arm description:

Subjects received GUS (guselkumab) 100 milligrams (mg) subcutaneously (SC) at Weeks 0 and 4, then every 8 weeks 12, 20, 28, 36, through Week (Wk) 44 with placebo SC administered at Week 24. At Week 16, subjects who met the early escape (EE) criteria received placebo at Week 16 and guselkumab at Week 20, then guselkumab every 8 weeks (q8w).

Arm type	Active comparator
Investigational medicinal product name	Guselkumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received guselkumab 100 mg SC at pre-specified timepoints.

Arm title	Group 2: Placebo

Arm description:

Subjects received placebo subcutaneously (SC) at Weeks 0, 4, 12, and 20 and crossed over at Week 24 to guselkumab SC 100 mg administered at Weeks 24, 28, 36, and 44. At Week 16, subjects who met the EE criteria received guselkumab at Week 16 and 20, then guselkumab q8w.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received placebo SC at pre-specified timepoints.

Number of subjects in period 1	Group 1: Guselkumab 100 mg q8w	Group 2: Placebo
Started	189	96
EE at Week 16	39 [1]	45 [2]
Crossover at Week 24	0 [3]	51 [4]
Continuing GUS at Week 24-56	174	0 [5]
Completed	167	83
Not completed	22	13
Consent withdrawn by subject	5	3
Adverse event, non-fatal	7	3
Unspecified	3	1
Lost to follow-up	1	1
Initiated prohibited medications	1	2
Lack of efficacy	5	3

Notes:

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

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

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

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

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

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: Guselkumab 100 mg q8w
Reporting group description:	
Subjects received GUS (guselkumab) 100 milligrams (mg) subcutaneously (SC) at Weeks 0 and 4, then every 8 weeks 12, 20, 28, 36, through Week (Wk) 44 with placebo SC administered at Week 24. At Week 16, subjects who met the early escape (EE) criteria received placebo at Week 16 and guselkumab at Week 20, then guselkumab every 8 weeks (q8w).	
Reporting group title	Group 2: Placebo
Reporting group description:	
Subjects received placebo subcutaneously (SC) at Weeks 0, 4, 12, and 20 and crossed over at Week 24 to guselkumab SC 100 mg administered at Weeks 24, 28, 36, and 44. At Week 16, subjects who met the EE criteria received guselkumab at Week 16 and 20, then guselkumab q8w.	

Reporting group values	Group 1: Guselkumab 100 mg q8w	Group 2: Placebo	Total
Number of subjects	189	96	285
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	169	89	258
From 65 to 84 years	20	7	27
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	49.1	49.1	
standard deviation	± 12.31	± 12.14	-
Title for Gender Units: subjects			
Female	103	44	147
Male	86	52	138

End points

End points reporting groups

Reporting group title	Group 1: Guselkumab 100 mg q8w

Reporting group description:

Subjects received GUS (guselkumab) 100 milligrams (mg) subcutaneously (SC) at Weeks 0 and 4, then every 8 weeks 12, 20, 28, 36, through Week (Wk) 44 with placebo SC administered at Week 24. At Week 16, subjects who met the early escape (EE) criteria received placebo at Week 16 and guselkumab at Week 20, then guselkumab every 8 weeks (q8w).

Reporting group title	Group 2: Placebo

Reporting group description:

Subjects received placebo subcutaneously (SC) at Weeks 0, 4, 12, and 20 and crossed over at Week 24 to guselkumab SC 100 mg administered at Weeks 24, 28, 36, and 44. At Week 16, subjects who met the EE criteria received guselkumab at Week 16 and 20, then guselkumab q8w.

Primary: Percentage of Subjects who Achieved an American College of Rheumatology (ACR) 20 Response at Week 24

End point title	Percentage of Subjects who Achieved an American College of Rheumatology (ACR) 20 Response at Week 24

End point description:

ACR 20 response is defined as greater than or equal to (>=)20 percent (%) improvement from baseline in tender joint count (68 joints) and swollen joint count (66 joints) and in 3 of following 5 assessments: Subject's assessment of pain Visual Analog Scale (VAS) 0-100 millimeter(mm) scale, 0=no pain to 100=worst possible pain, Subject's global assessment of disease activity (VAS)(scale, 0=Excellent to 100=poor), Physician's global assessment of disease activity (VAS) (scale, 0=no arthritis activity to 100=extremely active arthritis),Subject's assessment of physical function as measured by Health Assessment Questionnaire-Disability Index (HAQ-DI) (scale, 0=no difficulty to 3=inability to do task in that area), Serum C-reactive protein (CRP). Full Analysis Set 1 (FAS1) included all randomized subjects who received at least 1 dose (complete or partial) of study intervention. Subjects set to non-responders if they met treatment failure (TF) or had data missing.

End point type	Primary

End point timeframe:

Week 24

End point values	Group 1: Guselkumab 100 mg q8w	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	96		
Units: percentage of subjects				
number (not applicable)	44.4	19.8		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Group 1: Guselkumab 100 mg q8w v Group 2: Placebo

Number of subjects included in analysis	285
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	% difference
Point estimate	24.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.1
upper limit	35.2

Secondary: Change from Baseline in HAQ-DI Score at Week 24

End point title	Change from Baseline in HAQ-DI Score at Week 24

End point description:

The HAQ-DI measures the functional status of subjects scored on a scale of 0 to 3, with lower scores indicating better physical functioning. The 20-question instrument assesses the degree of difficulty a person has in accomplishing tasks in 8 functional areas (dressing, arising, eating, walking, hygiene, reaching, gripping, and activities of daily living). Responses in each functional area were scored from 0, indicating no difficulty, to 3, indicating inability to perform a task in that area. Overall score was computed as the sum of domain scores and divided by the number of domains answered. Total possible score range: 0-3 where 0 = least difficulty and 3 = extreme difficulty. FAS1 included all randomized subjects who received at least 1 dose (complete or partial) of study intervention. Subjects set to non-responders if they met TF or had missing data.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Group 1: Guselkumab 100 mg q8w	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	96		
Units: Units on a scale				
least squares mean (confidence interval 95%)	-0.178 (-0.269 to -0.086)	-0.009 (-0.120 to 0.102)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Group 1: Guselkumab 100 mg q8w v Group 2: Placebo

Number of subjects included in analysis	285
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Mixed model for repeated measures
Parameter estimate	LS mean Difference
Point estimate	-0.169
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.279
upper limit	-0.059

Secondary: Percentage of Subjects who Achieved an ACR 50 Response at Week 24

End point title	Percentage of Subjects who Achieved an ACR 50 Response at Week 24

End point description:

ACR 50 response is defined as >=50% improvement from baseline in tender joint count (68 joints) and swollen joint count (66 joints) and in 3 of following 5 assessments: Subject's assessment of pain (VAS) 0-100mm scale, 0=no pain to 100=worst possible pain, Subject's global assessment of disease activity (VAS) (scale, 0=Excellent to 100=poor), Physician's global assessment of disease activity (VAS) (scale, 0=no arthritis activity to 100=extremely active arthritis), Subject's assessment of physical function as measured by HAQ-DI (scale, 0=no difficulty to 3=inability to do task in that area), CRP. FAS1 included all randomized subjects who received at least 1 dose (complete or partial) of study intervention. Subjects set to non-responders if they met TF or had missing data.

End point type	Secondary

End point timeframe:

Week 24

End point values	Group 1: Guselkumab 100 mg q8w	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	96		
Units: percentage of subjects				
number (not applicable)	19.6	5.2		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Group 1: Guselkumab 100 mg q8w v Group 2: Placebo

Number of subjects included in analysis	285
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	% difference
Point estimate	14.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.2
upper limit	21.4

Secondary: Change from Baseline in Physical Component Summary Scores (PCS) of the in 36-Item Short form Health Survey (SF-36) Score at Week 24

End point title	Change from Baseline in Physical Component Summary Scores (PCS) of the in 36-Item Short form Health Survey (SF-36) Score at Week 24

End point description:

The SF-36 is a generic health survey with 36 items that measure functional health and well-being from the participant's perspective. The survey is summarized into 8 dimensions/scales: physical functioning (PF), role-physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role-emotional (RE), and mental health (MH). The physical component summary measure is derived from 4 of the 8 health dimensions (aggregate of PF, RP, BP, and GH scales). The minimum score is 0 and the maximum score is 100. A higher score indicates a better health state. FAS1 included all randomized subjects who received at least 1 dose (complete or partial) of study intervention. Subjects set to non-responders if they met TF or had missing data. Here 'n' (number analyzed) included all subjects who were analyzed at the specified timepoint.

End point type	Secondary

End point timeframe:

Week 24

End point values	Group 1: Guselkumab 100 mg q8w	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	188	96		
Units: Units on a scale				
least squares mean (confidence interval 95%)	3.514 (2.314 to 4.715)	-0.387 (-1.841 to 1.067)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Group 1: Guselkumab 100 mg q8w v Group 2: Placebo

Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed model for repeated measures (MMRM)
Parameter estimate	LS mean difference
Point estimate	3.901
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.457
upper limit	5.346

Secondary: Percentage of Subjects who Achieve Psoriatic Area and Severity Index (PASI) 100 Response at Week 24 Among Subjects with >=3% body Surface area Psoriatic Involvement and an Investigator's Global Assessment (IGA) Score of >=2 (Mild) at Baseline

End point title	Percentage of Subjects who Achieve Psoriatic Area and Severity Index (PASI) 100 Response at Week 24 Among Subjects with >=3% body Surface area Psoriatic Involvement and an Investigator's Global Assessment (IGA) Score of >=2 (Mild) at Baseline

End point description:

The PASI is a system used for assessing and grading severity of psoriatic lesions and their response to therapy. The PASI produces a numeric score that can range from 0 (no disease) to 72 (maximal disease). PASI 100 response is defined as 100 percent (%) improvement in PASI score from baseline. Population analyzed included FAS1 among the subjects who had >=3% body surface area (BSA) of Psoriatic involvement and an IGA Score >=2 (mild) at baseline. Subjects set to non-responders if they met TF or had missing data. Here 'n' (number analyzed) included all subjects who were analyzed at the specified timepoint.

End point type	Secondary

End point timeframe:

Week 24

End point values	Group 1: Guselkumab 100 mg q8w	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	133	53		
Units: percentage of subjects				
number (not applicable)	30.8	3.8		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Group 1: Guselkumab 100 mg q8w v Group 2: Placebo

Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	% difference
Point estimate	27.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.9
upper limit	36.8

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Week 56

Adverse event reporting additional description:

The Safety Analysis Set 2 (SAS2) included all subjects who received at least 1 (complete or partial) dose of guselkumab from Week 0 to Week 56.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Placebo Early Escape crossover to Guselkumab at Week 16

Reporting group description:

Subjects received placebo and switched to guselkumab treatment at Week 16 (Early Escape Route), from the date of the first guselkumab administration up to End of Study (Week 56).

Reporting group title	Placebo No Early Escape crossover to Guselkumab at Week 24

Reporting group description:

Subjects received placebo and switched to guselkumab treatment at Week 24, from the date of the first guselkumab administration up to End of Study (Week 56).

Reporting group title	Randomized to Guselkumab Week 0 to Week 24

Reporting group description:

Subjects randomized to guselkumab treatment, from the date of the first guselkumab administration up to (but not including) the date of the Week 24 visit.

Reporting group title	Randomized to Guselkumab Week 24 to Week 56

Reporting group description:

Subjects randomized to guselkumab treatment, starting at the date of the Week 24 visit up to end of study (Week 56).

Reporting group title	Guselkumab Combined

Reporting group description:

Subjects received at least 1 dose of guselkumab including those randomized to receive guselkumab at Week 0, those who switched to guselkumab treatment at Week 16, and those who switched to guselkumab treatment at Week 24.

Serious adverse events	Placebo Early Escape crossover to Guselkumab at Week 16	Placebo No Early Escape crossover to Guselkumab at Week 24	Randomized to Guselkumab Week 0 to Week 24
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 45 (4.44%)	2 / 45 (4.44%)	7 / 189 (3.70%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 189 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hepatic Enzyme Increased			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 189 (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
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate Cancer			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 189 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Buttock Injury			
subjects affected / exposed	1 / 45 (2.22%)	0 / 45 (0.00%)	0 / 189 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Varicose Vein			
subjects affected / exposed	1 / 45 (2.22%)	0 / 45 (0.00%)	0 / 189 (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
Cardiac disorders			
Acute Coronary Syndrome			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 189 (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
Atrial Fibrillation			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 189 (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			
Lumbosacral Radiculopathy			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 189 (0.53%)
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			

Abdominal Pain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 189 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary Embolism			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 189 (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			
Conversion Disorder			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 189 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 189 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral Disc Protrusion			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 189 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	1 / 189 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Randomized to Guselkumab Week 24 to Week 56	Guselkumab Combined	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 174 (2.87%)	15 / 279 (5.38%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 174 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic Enzyme Increased			
subjects affected / exposed	0 / 174 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate Cancer			
subjects affected / exposed	0 / 174 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Buttock Injury			
subjects affected / exposed	0 / 174 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Varicose Vein			
subjects affected / exposed	0 / 174 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute Coronary Syndrome			
subjects affected / exposed	1 / 174 (0.57%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial Fibrillation			
subjects affected / exposed	1 / 174 (0.57%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			

Lumbosacral Radiculopathy			
subjects affected / exposed	0 / 174 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	1 / 174 (0.57%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary Embolism			
subjects affected / exposed	1 / 174 (0.57%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Conversion Disorder			
subjects affected / exposed	1 / 174 (0.57%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 174 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral Disc Protrusion			
subjects affected / exposed	0 / 174 (0.00%)	1 / 279 (0.36%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 174 (0.00%)	2 / 279 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo Early Escape crossover to Guselkumab at Week 16	Placebo No Early Escape crossover to Guselkumab at Week 24	Randomized to Guselkumab Week 0 to Week 24
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 45 (6.67%)	3 / 45 (6.67%)	14 / 189 (7.41%)
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 45 (2.22%)	3 / 45 (6.67%)	4 / 189 (2.12%)
occurrences (all)	1	5	4
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 45 (4.44%)	0 / 45 (0.00%)	10 / 189 (5.29%)
occurrences (all)	2	0	10

Non-serious adverse events	Randomized to Guselkumab Week 24 to Week 56	Guselkumab Combined	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 174 (4.60%)	26 / 279 (9.32%)	
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	3 / 174 (1.72%)	10 / 279 (3.58%)	
occurrences (all)	3	13	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 174 (2.87%)	16 / 279 (5.73%)	
occurrences (all)	5	17	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 September 2019	It was implemented to clarify the definition of the Safety Analysis Set, to indicate that nominal, unadjusted analyses could be done for major secondary endpoints, to indicate that biomarker sampling at screening was optional, and to add clarity to the timing of certain assessments relative to dosing.
28 April 2020	It was implemented to provide guidance on study conduct and assessments during the Coronavirus Disease-2019 (COVID-19) pandemic. This amendment secured the possibility of SC injections of study intervention to be self-administered or be given by a caregiver/healthcare provider professional/site staff outside a study-site after Week 24, in cases where a site visit was not possible in view of national, regional or local restrictions.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

20 subjects were incorrectly routed to early escape (EE) at Week 16. Supplementary analysis 1 was done regardless of treatment used at that time-point and included all subjects in placebo group,even if they switched to guselkumab at Week 16 or not.

Notes: