# 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<br>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<br>Units: years | | | |
| arithmetic mean | 49.1 | 49.1 | |
| standard deviation | ± 12.31 | ± 12.14 | - |
| Title for Gender<br>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<br>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: