



Clinical trial results:

A 24-week, randomized, double-blind, placebo-controlled, multicenter study to evaluate the efficacy and safety of secukinumab in controlling spinal pain in patients with axial spondyloarthritis

Summary

| | |
|--------------------------|--|
| EudraCT number | 2017-000401-21 |
| Trial protocol | ES CZ FI GB LV LT GR BE SE BG PL HR IT |
| Global end of trial date | 15 February 2019 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 |
| This version publication date | 21 February 2020 |
| First version publication date | 21 February 2020 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | CAIN457H3301 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03136861 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Novartis Pharma AG |
| Sponsor organisation address | CH-4002, Basel, Switzerland, |
| Public contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com |
| Scientific contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.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 | 15 February 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 15 February 2019 |
| Global end of trial reached? | Yes |
| Global end of trial date | 15 February 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the superiority of secukinumab 150 mg compared to placebo in achieving a spinal pain score of < 4 on a 0-10 numerical rating scale (NRS) at Week 8.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 30 June 2017 |
| 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: 10 |
| Country: Number of subjects enrolled | Bulgaria: 17 |
| Country: Number of subjects enrolled | Croatia: 11 |
| Country: Number of subjects enrolled | Czech Republic: 21 |
| Country: Number of subjects enrolled | Estonia: 24 |
| Country: Number of subjects enrolled | Finland: 8 |
| Country: Number of subjects enrolled | United Kingdom: 11 |
| Country: Number of subjects enrolled | Greece: 21 |
| Country: Number of subjects enrolled | Ireland: 6 |
| Country: Number of subjects enrolled | Italy: 1 |
| Country: Number of subjects enrolled | Latvia: 16 |
| Country: Number of subjects enrolled | Lithuania: 26 |
| Country: Number of subjects enrolled | Poland: 116 |
| Country: Number of subjects enrolled | Russian Federation: 38 |
| Country: Number of subjects enrolled | Spain: 42 |
| Country: Number of subjects enrolled | Sweden: 6 |
| Country: Number of subjects enrolled | Switzerland: 6 |
| Worldwide total number of subjects | 380 |
| EEA total number of subjects | 336 |

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) | 368 |
| From 65 to 84 years | 12 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 66 centers in 17 countries worldwide: Spain(14), Czech Republic(3), Finland(2), Lithuania(2), Estonia(3), Latvia(3), Switzerland(1), Russia(4), Sweden(4), United Kingdom(5), Belgium(2), Ireland(2), Poland(7), Croatia(3), Bulgaria(5), Greece(5), Italy(1).

Pre-assignment

Screening details:

At Baseline, patients were randomized to either secukinumab 150 mg or placebo (Group A or B). At Week 8, patients were re-randomized or re-assigned respectively to 1 of 5 treatment arms to receive either secukinumab 150 mg or secukinumab 300 mg (Arm A1 to B2).

Period 1

| | |
|------------------------------|---|
| Period 1 title | Treatment Period 1 (TP1)(Baseline-Wk 8) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Carer, Assessor |

Arms

| | |
|------------------------------|------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Secukinumab 150 mg (Group A) |

Arm description:

Treatment Period 1: Secukinumab 150 mg (1 x 1.0 mL) s.c. administered at Baseline, Week 1, 2, 3 and 4

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | AIN457 |
| Investigational medicinal product code | |
| Other name | Secukinumab |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Secukinumab sc injections weekly up to week 4.

| | |
|------------------|-------------------|
| Arm title | Placebo (Group B) |
|------------------|-------------------|

Arm description:

Treatment Period 1: Placebo (1 x 1.0 mL) s.c. administered at Baseline and Week 1, 2, 3 and 4

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

Dosage and administration details:

Placebo sc injections weekly up to week 4.

| Number of subjects in period 1 | Secukinumab 150 mg (Group A) | Placebo (Group B) |
|--------------------------------|------------------------------|-------------------|
| Started | 285 | 95 |
| Completed | 278 | 89 |
| Not completed | 7 | 6 |
| Adverse event, non-fatal | 3 | 2 |
| Protocol Deviation | 2 | 1 |
| Subject/Guardian Decision | - | 1 |
| Lost to follow-up | 1 | 1 |
| Withdrawal of Informed Consent | 1 | 1 |

Period 2

| | |
|------------------------------|--|
| Period 2 title | Treatment Period 2 (TP2) (Wk 8-Wk 24) |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Carer, Assessor |

Arms

| | |
|------------------------------|--------|
| Are arms mutually exclusive? | Yes |
| Arm title | Arm A1 |

Arm description:

Treatment Period 2: Secukinumab 150 mg (1 x 1.0 mL) plus placebo (1 x 1.0 mL) administered at Week 8, 12, 16 and 20

| | |
|--|--|
| Arm type | Active comparator |
| Investigational medicinal product name | AIN457 |
| Investigational medicinal product code | |
| Other name | Secukinumab |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Secukinumab sc injections every 4 weeks between week 8 and week 20.

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

Dosage and administration details:

Placebo sc injections every 4 weeks between week 8 and week 20.

| | |
|------------------|--------|
| Arm title | Arm A2 |
|------------------|--------|

Arm description:

Treatment Period 2: Secukinumab 150 mg (1 x 1.0 mL) plus placebo (1 x 1.0 mL) administered at Week 8, 12, 16 and 20

| | |
|----------|-------------------|
| Arm type | Active comparator |
|----------|-------------------|

| | |
|---|--|
| Investigational medicinal product name | AIN457 |
| Investigational medicinal product code | |
| Other name | Secukinumab |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| Secukinumab sc injections every 4 weeks between week 8 and week 20. | |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | Placebo |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| Placebo sc injections every 4 weeks between week 8 and week 20. | |
| Arm title | Arm A3 |
| Arm description: | |
| Treatment Period 2: Secukinumab 300 mg (2 x 1.0 mL) administered at Week 8, 12, 16, and 20 | |
| Arm type | Active comparator |
| Investigational medicinal product name | AIN457 |
| Investigational medicinal product code | |
| Other name | Secukinumab |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| 2 secukinumab sc injections every 4 weeks between week 8 and week 20. | |
| Arm title | Arm B1 |
| Arm description: | |
| Treatment Period 2: Secukinumab 150 mg (1 x 1.0 mL) plus placebo (1 x 1.0 mL) administered at Week 8, 12, 16 and 20 | |
| Arm type | Active comparator |
| Investigational medicinal product name | AIN457 |
| Investigational medicinal product code | |
| Other name | Secukinumab |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| Secukinumab sc injections every 4 weeks between week 8 and week 20. | |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | Placebo |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: | |
| Placebo sc injections every 4 weeks between week 8 and week 20. | |
| Arm title | Arm B2 |
| Arm description: | |
| Treatment Period 2: Secukinumab 300 mg (2 x 1.0 mL) administered at Week 8, 12, 16, and 20 | |
| Arm type | Active comparator |

| | |
|--|--|
| Investigational medicinal product name | AIN457 |
| Investigational medicinal product code | |
| Other name | Secukinumab |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

2 secukinumab sc injections every 4 weeks between week 8 and week 20.

| Number of subjects in period 2 | Arm A1 | Arm A2 | Arm A3 |
|---------------------------------------|--------|--------|--------|
| Started | 90 | 94 | 94 |
| Completed | 88 | 93 | 92 |
| Not completed | 2 | 1 | 2 |
| Adverse event, non-fatal | - | 1 | 2 |
| Lost to follow-up | 1 | - | - |
| Withdrawal of Informed Consent | 1 | - | - |

| Number of subjects in period 2 | Arm B1 | Arm B2 |
|---------------------------------------|--------|--------|
| Started | 45 | 44 |
| Completed | 45 | 43 |
| Not completed | 0 | 1 |
| Adverse event, non-fatal | - | 1 |
| Lost to follow-up | - | - |
| Withdrawal of Informed Consent | - | - |

Baseline characteristics

Reporting groups

| | |
|---|------------------------------|
| Reporting group title | Secukinumab 150 mg (Group A) |
| Reporting group description: | |
| Treatment Period 1: Secukinumab 150 mg (1 x 1.0 mL) s.c. administered at Baseline, Week 1, 2, 3 and 4 | |
| Reporting group title | Placebo (Group B) |
| Reporting group description: | |
| Treatment Period 1: Placebo (1 x 1.0 mL) s.c. administered at Baseline and Week 1, 2, 3 and 4 | |

| Reporting group values | Secukinumab 150 mg (Group A) | Placebo (Group B) | Total |
|--|------------------------------|-------------------|-------|
| Number of subjects | 285 | 95 | 380 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 274 | 94 | 368 |
| From 65-84 years | 11 | 1 | 12 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous | | | |
| Age continuous at Baseline Treatment Period 1 | | | |
| Units: Years | | | |
| arithmetic mean | 42.3 | 40.9 | |
| standard deviation | ± 11.88 | ± 12.20 | - |
| Sex: Female, Male | | | |
| Gender at Baseline Treatment Period 1 | | | |
| Units: Participants | | | |
| Female | 106 | 39 | 145 |
| Male | 179 | 56 | 235 |
| Race/Ethnicity, Customized | | | |
| Race at Baseline Treatment Period 1 | | | |
| Units: Subjects | | | |
| Caucasian | 267 | 93 | 360 |
| Asian | 2 | 1 | 3 |
| Other | 16 | 1 | 17 |

End points

End points reporting groups

| | |
|---|------------------------------|
| Reporting group title | Secukinumab 150 mg (Group A) |
| Reporting group description: | |
| Treatment Period 1: Secukinumab 150 mg (1 x 1.0 mL) s.c. administered at Baseline, Week 1, 2, 3 and 4 | |
| Reporting group title | Placebo (Group B) |
| Reporting group description: | |
| Treatment Period 1: Placebo (1 x 1.0 mL) s.c. administered at Baseline and Week 1, 2, 3 and 4 | |
| Reporting group title | Arm A1 |
| Reporting group description: | |
| Treatment Period 2: Secukinumab 150 mg (1 x 1.0 mL) plus placebo (1 x 1.0 mL) administered at Week 8, 12, 16 and 20 | |
| Reporting group title | Arm A2 |
| Reporting group description: | |
| Treatment Period 2: Secukinumab 150 mg (1 x 1.0 mL) plus placebo (1 x 1.0 mL) administered at Week 8, 12, 16 and 20 | |
| Reporting group title | Arm A3 |
| Reporting group description: | |
| Treatment Period 2: Secukinumab 300 mg (2 x 1.0 mL) administered at Week 8, 12, 16, and 20 | |
| Reporting group title | Arm B1 |
| Reporting group description: | |
| Treatment Period 2: Secukinumab 150 mg (1 x 1.0 mL) plus placebo (1 x 1.0 mL) administered at Week 8, 12, 16 and 20 | |
| Reporting group title | Arm B2 |
| Reporting group description: | |
| Treatment Period 2: Secukinumab 300 mg (2 x 1.0 mL) administered at Week 8, 12, 16, and 20 | |

Primary: Percentage of participants with a spinal pain numerical rating scale (NRS) score below 4 at Week 8

| | |
|---|--|
| End point title | Percentage of participants with a spinal pain numerical rating scale (NRS) score below 4 at Week 8 |
| End point description: | |
| The spinal pain numerical rating scale (NRS) is an 11-point scale to assess pain intensity in patients who are able to self-report. To calculate the average spinal pain, the patient is asked to answer 2 questions to get 2 pain ratings, the total spinal pain corresponding to the intensity of spinal pain experienced on an average over 24 hours during the previous week and the nocturnal back pain corresponding to the intensity of spinal pain experienced on an average over the night during the previous week. | |
| End point type | Primary |
| End point timeframe: | |
| Week 8 | |

| End point values | Secukinumab 150 mg (Group A) | Placebo (Group B) | | |
|---------------------------------|------------------------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 279 | 92 | | |
| Units: Participants | | | | |
| Average Spinal Pain Score Yes | 91 | 19 | | |
| Total Spinal Pain Score Yes | 92 | 16 | | |
| Nocturnal Spinal Pain Score Yes | 77 | 17 | | |
| Average Spinal Pain Score No | 188 | 73 | | |
| Total Spinal Pain Score No | 187 | 76 | | |
| Nocturnal Spinal Pain Score No | 202 | 75 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Average Spinal Pain Score <4 at Week 8 |
| Comparison groups | Secukinumab 150 mg (Group A) v Placebo (Group B) |
| Number of subjects included in analysis | 371 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0264 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.89 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.08 |
| upper limit | 3.33 |

| | |
|---|--|
| Statistical analysis title | Total Spinal Pain Score <4 at Week 8 |
| Comparison groups | Secukinumab 150 mg (Group A) v Placebo (Group B) |
| Number of subjects included in analysis | 371 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0043 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.38 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.31 |
| upper limit | 4.31 |

| | |
|---|--|
| Statistical analysis title | Nocturnal Spinal Pain Score |
| Comparison groups | Secukinumab 150 mg (Group A) v Placebo (Group B) |
| Number of subjects included in analysis | 371 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.072 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.72 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.95 |
| upper limit | 3.1 |

Secondary: Percentage of participants with a Bath ankylosing spondylitis disease activity index score below 4 at Week 8

| | |
|--|--|
| End point title | Percentage of participants with a Bath ankylosing spondylitis disease activity index score below 4 at Week 8 |
| End point description: The Bath ankylosing spondylitis disease activity index (BASDAI) consists of a 0 through 10 scale, which is used to answer 6 questions pertaining to the 5 major symptoms of ankylosing spondylitis. To give each symptom equal weighting, the mean (average) of the 2 scores relating to morning stiffness (questions 5 and 6) is taken. The mean of questions 5 and 6 is added to the scores from questions 1-4. The resulting 0 to 50 score is divided by 5 to give a final 0 – 10 BASDAI score. | |
| End point type | Secondary |
| End point timeframe: Week 8 | |

| End point values | Secukinumab 150 mg (Group A) | Placebo (Group B) | | |
|-----------------------------|------------------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 280 | 92 | | |
| Units: Participants | | | | |
| Yes (n=95,22) | 95 | 22 | | |
| No (n=185,70) | 185 | 70 | | |

Statistical analyses

| | |
|-----------------------------------|--|
| Statistical analysis title | BASDAI Score <4 at Week 8 |
| Comparison groups | Secukinumab 150 mg (Group A) v Placebo (Group B) |

| | |
|---|----------------------|
| Number of subjects included in analysis | 372 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0466 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.75 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.01 |
| upper limit | 3.04 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment emergent adverse events were collected from first dose of study treatment until end of study treatment plus 12 weeks, up to a maximum duration of 32 weeks.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 21.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | Secukinumab 150 mg |
|-----------------------|--------------------|

Reporting group description:

Treatment Period 1: Secukinumab 150 mg (1 x 1.0 mL) s.c. administered at Baseline, Week 1, 2, 3 and 4

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Treatment Period 1: Placebo (1 x 1.0 mL) s.c. administered at Baseline and Week 1, 2, 3 and 4

| | |
|-----------------------|--------|
| Reporting group title | Arm A1 |
|-----------------------|--------|

Reporting group description:

Treatment Period 2: Secukinumab 150 mg (1 x 1.0 mL) plus placebo (1 x 1.0 mL) administered at Week 8, 12, 16 and 20

| | |
|-----------------------|--------|
| Reporting group title | Arm A2 |
|-----------------------|--------|

Reporting group description:

Treatment Period 2: Secukinumab 150 mg (1 x 1.0 mL) plus placebo (1 x 1.0 mL) administered at Week 8, 12, 16 and 20

| | |
|-----------------------|--------|
| Reporting group title | Arm A3 |
|-----------------------|--------|

Reporting group description:

Treatment Period 2: Secukinumab 300 mg (2 x 1.0 mL) administered at Week 8, 12, 16, and 20

| | |
|-----------------------|--------|
| Reporting group title | Arm B1 |
|-----------------------|--------|

Reporting group description:

Treatment Period 2: Secukinumab 150 mg (1 x 1.0 mL) plus placebo (1 x 1.0 mL) administered at Week 8, 12, 16 and 20

| | |
|-----------------------|--------|
| Reporting group title | Arm B2 |
|-----------------------|--------|

Reporting group description:

Treatment Period 2: Secukinumab 300 mg (2 x 1.0 mL) administered at Week 8, 12, 16, and 20

| Serious adverse events | Secukinumab 150 mg | Placebo | Arm A1 |
|---|--------------------|----------------|----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 285 (1.40%) | 0 / 95 (0.00%) | 3 / 90 (3.33%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |

| | | | |
|---|-----------------|----------------|----------------|
| Malignant melanoma | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 95 (0.00%) | 0 / 90 (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 | | | |
| Facial bones fracture | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 95 (0.00%) | 0 / 90 (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 myocardial infarction | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 95 (0.00%) | 0 / 90 (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 | 1 / 285 (0.35%) | 0 / 95 (0.00%) | 0 / 90 (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 |
| Nervous system disorders | | | |
| Hemiparesis | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 95 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 95 (0.00%) | 1 / 90 (1.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 95 (0.00%) | 1 / 90 (1.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Renal impairment | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 95 (0.00%) | 1 / 90 (1.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal mass | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 95 (0.00%) | 0 / 90 (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 |
| Infections and infestations | | | |
| Anal abscess | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 95 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Arm A2 | Arm A3 | Arm B1 |
|---|----------------|----------------|----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 94 (1.06%) | 1 / 94 (1.06%) | 0 / 45 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Malignant melanoma | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | 1 / 94 (1.06%) | 0 / 45 (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 |
| Injury, poisoning and procedural complications | | | |
| Facial bones fracture | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | 0 / 94 (0.00%) | 0 / 45 (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 / 94 (0.00%) | 0 / 94 (0.00%) | 0 / 45 (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 |
| Myocardial infarction | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 94 (0.00%) | 0 / 94 (0.00%) | 0 / 45 (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 | | | |
| Hemiparesis | | | |
| subjects affected / exposed | 1 / 94 (1.06%) | 0 / 94 (0.00%) | 0 / 45 (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 |
| Gastrointestinal disorders | | | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | 0 / 94 (0.00%) | 0 / 45 (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 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | 0 / 94 (0.00%) | 0 / 45 (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 |
| Renal and urinary disorders | | | |
| Renal impairment | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | 0 / 94 (0.00%) | 0 / 45 (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 |
| Renal mass | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | 0 / 94 (0.00%) | 0 / 45 (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 | 0 / 94 (0.00%) | 0 / 94 (0.00%) | 0 / 45 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Serious adverse events | | | |
| Arm B2 | | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | | |

| | | | |
|---|----------------|--|--|
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Malignant melanoma | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Facial bones fracture | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Hemiparesis | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| Renal and urinary disorders | | | |
| Renal impairment | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal mass | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Anal abscess | | | |
| subjects affected / exposed | 0 / 44 (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: 2 %

| Non-serious adverse events | Secukinumab 150 mg | Placebo | Arm A1 |
|---|--------------------|------------------|------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 59 / 285 (20.70%) | 23 / 95 (24.21%) | 21 / 90 (23.33%) |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 3 / 285 (1.05%) | 1 / 95 (1.05%) | 0 / 90 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 6 / 285 (2.11%) | 0 / 95 (0.00%) | 1 / 90 (1.11%) |
| occurrences (all) | 6 | 0 | 1 |
| Injection site pain | | | |
| subjects affected / exposed | 2 / 285 (0.70%) | 0 / 95 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Vulvovaginal pruritus | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 95 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|-----------------|----------------|----------------|
| Respiratory, thoracic and mediastinal disorders | | | |
| Bronchospasm | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 95 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cough | | | |
| subjects affected / exposed | 2 / 285 (0.70%) | 0 / 95 (0.00%) | 3 / 90 (3.33%) |
| occurrences (all) | 2 | 0 | 3 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 8 / 285 (2.81%) | 1 / 95 (1.05%) | 4 / 90 (4.44%) |
| occurrences (all) | 9 | 1 | 4 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 1 / 95 (1.05%) | 0 / 90 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 95 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 1 / 95 (1.05%) | 0 / 90 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 4 / 285 (1.40%) | 0 / 95 (0.00%) | 3 / 90 (3.33%) |
| occurrences (all) | 4 | 0 | 3 |
| Injury, poisoning and procedural complications | | | |
| Arthropod bite | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 95 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 1 / 95 (1.05%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Limb injury | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 95 (0.00%) | 2 / 90 (2.22%) |
| occurrences (all) | 1 | 0 | 2 |
| Nervous system disorders | | | |

| | | | |
|---|------------------------|---------------------|---------------------|
| Headache subjects affected / exposed occurrences (all) | 10 / 285 (3.51%) 12 | 1 / 95 (1.05%) 1 | 2 / 90 (2.22%) 2 |
| Blood and lymphatic system disorders Neutropenia subjects affected / exposed occurrences (all) | 1 / 285 (0.35%) 1 | 1 / 95 (1.05%) 1 | 1 / 90 (1.11%) 1 |
| Ear and labyrinth disorders Deafness subjects affected / exposed occurrences (all) | 0 / 285 (0.00%) 0 | 0 / 95 (0.00%) 0 | 0 / 90 (0.00%) 0 |
| Eye disorders Blepharitis subjects affected / exposed occurrences (all) | 0 / 285 (0.00%) 0 | 0 / 95 (0.00%) 0 | 0 / 90 (0.00%) 0 |
| Iritis subjects affected / exposed occurrences (all) | 0 / 285 (0.00%) 0 | 0 / 95 (0.00%) 0 | 0 / 90 (0.00%) 0 |
| Vitreous haemorrhage subjects affected / exposed occurrences (all) | 0 / 285 (0.00%) 0 | 0 / 95 (0.00%) 0 | 0 / 90 (0.00%) 0 |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) | 3 / 285 (1.05%) 3 | 1 / 95 (1.05%) 1 | 0 / 90 (0.00%) 0 |
| Diarrhoea subjects affected / exposed occurrences (all) | 6 / 285 (2.11%) 9 | 1 / 95 (1.05%) 1 | 0 / 90 (0.00%) 0 |
| Frequent bowel movements subjects affected / exposed occurrences (all) | 0 / 285 (0.00%) 0 | 0 / 95 (0.00%) 0 | 0 / 90 (0.00%) 0 |
| Toothache subjects affected / exposed occurrences (all) | 0 / 285 (0.00%) 0 | 0 / 95 (0.00%) 0 | 0 / 90 (0.00%) 0 |
| Hepatobiliary disorders Hypertransaminasaemia | | | |

| | | | |
|---|--|---|---|
| subjects affected / exposed occurrences (all) | 1 / 285 (0.35%) 1 | 0 / 95 (0.00%) 0 | 0 / 90 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) | 2 / 285 (0.70%) 2 | 0 / 95 (0.00%) 0 | 0 / 90 (0.00%) 0 |
| Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all) Proteinuria subjects affected / exposed occurrences (all) | 1 / 285 (0.35%) 1 3 / 285 (1.05%) 3 | 0 / 95 (0.00%) 0 1 / 95 (1.05%) 1 | 1 / 90 (1.11%) 1 0 / 90 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Ankylosing spondylitis subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Bursitis subjects affected / exposed occurrences (all) Foot deformity subjects affected / exposed occurrences (all) Muscle contracture subjects affected / exposed occurrences (all) Osteoarthritis subjects affected / exposed occurrences (all) Pain in extremity | 0 / 285 (0.00%) 0 4 / 285 (1.40%) 4 1 / 285 (0.35%) 1 1 / 285 (0.35%) 1 0 / 285 (0.00%) 0 0 / 285 (0.00%) 0 0 / 285 (0.00%) 0 0 / 285 (0.00%) 0 | 0 / 95 (0.00%) 0 2 / 95 (2.11%) 2 3 / 95 (3.16%) 5 0 / 95 (0.00%) 0 0 / 95 (0.00%) 0 0 / 95 (0.00%) 0 0 / 95 (0.00%) 0 | 0 / 90 (0.00%) 0 0 / 90 (0.00%) 0 0 / 90 (0.00%) 0 1 / 90 (1.11%) 1 0 / 90 (0.00%) 0 0 / 90 (0.00%) 0 0 / 90 (0.00%) 0 |

| | | | |
|--|----------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 6 / 285 (2.11%) 6 | 0 / 95 (0.00%) 0 | 1 / 90 (1.11%) 1 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 1 / 95 (1.05%) | 1 / 90 (1.11%) |
| occurrences (all) | 0 | 1 | 1 |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 95 (0.00%) | 2 / 90 (2.22%) |
| occurrences (all) | 0 | 0 | 2 |
| Herpes simplex | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 95 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 6 / 285 (2.11%) | 1 / 95 (1.05%) | 1 / 90 (1.11%) |
| occurrences (all) | 7 | 1 | 1 |
| Otitis externa | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 95 (0.00%) | 1 / 90 (1.11%) |
| occurrences (all) | 1 | 0 | 2 |
| Pharyngitis | | | |
| subjects affected / exposed | 3 / 285 (1.05%) | 0 / 95 (0.00%) | 2 / 90 (2.22%) |
| occurrences (all) | 3 | 0 | 2 |
| Rhinitis | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 95 (0.00%) | 2 / 90 (2.22%) |
| occurrences (all) | 1 | 0 | 2 |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 2 / 95 (2.11%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 4 / 285 (1.40%) | 5 / 95 (5.26%) | 1 / 90 (1.11%) |
| occurrences (all) | 4 | 5 | 1 |
| Viral pharyngitis | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 95 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 95 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|------------------------------------|-----------------|----------------|----------------|
| Metabolism and nutrition disorders | | | |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 95 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lactose intolerance | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 95 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| Non-serious adverse events | Arm A2 | Arm A3 | Arm B1 |
|---|------------------|------------------|-----------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 24 / 94 (25.53%) | 23 / 94 (24.47%) | 9 / 45 (20.00%) |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | 0 / 94 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 94 (1.06%) | 0 / 94 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Injection site pain | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | 3 / 94 (3.19%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Reproductive system and breast disorders | | | |
| Vulvovaginal pruritus | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | 0 / 94 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Bronchospasm | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | 0 / 94 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cough | | | |
| subjects affected / exposed | 1 / 94 (1.06%) | 1 / 94 (1.06%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 2 / 94 (2.13%) | 0 / 94 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Rhinorrhoea | | | |

| | | | |
|--|---|---|---|
| subjects affected / exposed occurrences (all) | 0 / 94 (0.00%) 0 | 2 / 94 (2.13%) 2 | 0 / 45 (0.00%) 0 |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 2 / 94 (2.13%) 2 | 0 / 94 (0.00%) 0 | 0 / 45 (0.00%) 0 |
| Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) Blood creatinine increased subjects affected / exposed occurrences (all) | 1 / 94 (1.06%) 1 1 / 94 (1.06%) 1 | 2 / 94 (2.13%) 2 0 / 94 (0.00%) 0 | 1 / 45 (2.22%) 1 0 / 45 (0.00%) 0 |
| Injury, poisoning and procedural complications Arthropod bite subjects affected / exposed occurrences (all) Foot fracture subjects affected / exposed occurrences (all) Limb injury subjects affected / exposed occurrences (all) | 0 / 94 (0.00%) 0 0 / 94 (0.00%) 0 0 / 94 (0.00%) 0 | 0 / 94 (0.00%) 0 0 / 94 (0.00%) 0 0 / 94 (0.00%) 0 | 0 / 45 (0.00%) 0 1 / 45 (2.22%) 1 0 / 45 (0.00%) 0 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 2 / 94 (2.13%) 2 | 3 / 94 (3.19%) 3 | 0 / 45 (0.00%) 0 |
| Blood and lymphatic system disorders Neutropenia subjects affected / exposed occurrences (all) | 0 / 94 (0.00%) 0 | 0 / 94 (0.00%) 0 | 0 / 45 (0.00%) 0 |
| Ear and labyrinth disorders Deafness subjects affected / exposed occurrences (all) | 0 / 94 (0.00%) 0 | 0 / 94 (0.00%) 0 | 1 / 45 (2.22%) 1 |
| Eye disorders | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| Blepharitis subjects affected / exposed occurrences (all) | 2 / 94 (2.13%) 2 | 0 / 94 (0.00%) 0 | 0 / 45 (0.00%) 0 |
| Iritis subjects affected / exposed occurrences (all) | 0 / 94 (0.00%) 0 | 0 / 94 (0.00%) 0 | 1 / 45 (2.22%) 1 |
| Vitreous haemorrhage subjects affected / exposed occurrences (all) | 0 / 94 (0.00%) 0 | 0 / 94 (0.00%) 0 | 0 / 45 (0.00%) 0 |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) | 1 / 94 (1.06%) 1 | 0 / 94 (0.00%) 0 | 0 / 45 (0.00%) 0 |
| Diarrhoea subjects affected / exposed occurrences (all) | 0 / 94 (0.00%) 0 | 1 / 94 (1.06%) 1 | 0 / 45 (0.00%) 0 |
| Frequent bowel movements subjects affected / exposed occurrences (all) | 0 / 94 (0.00%) 0 | 0 / 94 (0.00%) 0 | 0 / 45 (0.00%) 0 |
| Toothache subjects affected / exposed occurrences (all) | 2 / 94 (2.13%) 2 | 1 / 94 (1.06%) 1 | 0 / 45 (0.00%) 0 |
| Hepatobiliary disorders Hypertransaminasaemia subjects affected / exposed occurrences (all) | 0 / 94 (0.00%) 0 | 1 / 94 (1.06%) 1 | 1 / 45 (2.22%) 1 |
| Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) | 0 / 94 (0.00%) 0 | 0 / 94 (0.00%) 0 | 1 / 45 (2.22%) 1 |
| Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all) | 0 / 94 (0.00%) 0 | 3 / 94 (3.19%) 3 | 1 / 45 (2.22%) 1 |
| Proteinuria subjects affected / exposed occurrences (all) | 2 / 94 (2.13%) 3 | 0 / 94 (0.00%) 0 | 0 / 45 (0.00%) 0 |

| | | | |
|---|----------------|----------------|----------------|
| Musculoskeletal and connective tissue disorders | | | |
| Ankylosing spondylitis | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | 0 / 94 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 1 |
| Arthralgia | | | |
| subjects affected / exposed | 3 / 94 (3.19%) | 1 / 94 (1.06%) | 0 / 45 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Back pain | | | |
| subjects affected / exposed | 2 / 94 (2.13%) | 0 / 94 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Bursitis | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | 0 / 94 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Foot deformity | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | 0 / 94 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle contracture | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | 0 / 94 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | 0 / 94 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 94 (1.06%) | 0 / 94 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 94 (1.06%) | 0 / 94 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 1 | 0 | 1 |
| Conjunctivitis | | | |
| subjects affected / exposed | 2 / 94 (2.13%) | 1 / 94 (1.06%) | 0 / 45 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Herpes simplex | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | 0 / 94 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 3 / 94 (3.19%) | 4 / 94 (4.26%) | 2 / 45 (4.44%) |
| occurrences (all) | 3 | 4 | 2 |
| Otitis externa | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | 0 / 94 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 2 / 94 (2.13%) | 0 / 94 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 2 / 94 (2.13%) | 0 / 94 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | 0 / 94 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | 3 / 94 (3.19%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Viral pharyngitis | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | 0 / 94 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 94 (1.06%) | 0 / 94 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | 0 / 94 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lactose intolerance | | | |
| subjects affected / exposed | 0 / 94 (0.00%) | 0 / 94 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|------------------|--|--|
| Non-serious adverse events | Arm B2 | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 13 / 44 (29.55%) | | |
| Vascular disorders | | | |

| | | | |
|---|--|--|--|
| Hypertension subjects affected / exposed occurrences (all) | 1 / 44 (2.27%) 1 | | |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Injection site pain subjects affected / exposed occurrences (all) | 0 / 44 (0.00%) 0 0 / 44 (0.00%) 0 | | |
| Reproductive system and breast disorders Vulvovaginal pruritus subjects affected / exposed occurrences (all) | 1 / 44 (2.27%) 1 | | |
| Respiratory, thoracic and mediastinal disorders Bronchospasm subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all) | 1 / 44 (2.27%) 1 0 / 44 (0.00%) 0 0 / 44 (0.00%) 0 0 / 44 (0.00%) 0 | | |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 0 / 44 (0.00%) 0 | | |
| Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) Blood creatinine increased | 0 / 44 (0.00%) 0 | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 2 / 44 (4.55%) 2 | | |
| Injury, poisoning and procedural complications | | | |
| Arthropod bite | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | | |
| occurrences (all) | 1 | | |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | | |
| occurrences (all) | 0 | | |
| Limb injury | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | | |
| occurrences (all) | 2 | | |
| Blood and lymphatic system disorders | | | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | | |
| occurrences (all) | 1 | | |
| Ear and labyrinth disorders | | | |
| Deafness | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | | |
| occurrences (all) | 0 | | |
| Eye disorders | | | |
| Blepharitis | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | | |
| occurrences (all) | 0 | | |
| Iritis | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vitreous haemorrhage | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |

| | | | |
|--|--|--|--|
| Abdominal pain subjects affected / exposed occurrences (all) | 1 / 44 (2.27%) 1 | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 0 / 44 (0.00%) 0 | | |
| Frequent bowel movements subjects affected / exposed occurrences (all) | 1 / 44 (2.27%) 1 | | |
| Toothache subjects affected / exposed occurrences (all) | 0 / 44 (0.00%) 0 | | |
| Hepatobiliary disorders Hypertransaminasaemia subjects affected / exposed occurrences (all) | 0 / 44 (0.00%) 0 | | |
| Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) | 0 / 44 (0.00%) 0 | | |
| Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all) Proteinuria subjects affected / exposed occurrences (all) | 0 / 44 (0.00%) 0 0 / 44 (0.00%) 0 | | |
| Musculoskeletal and connective tissue disorders Ankylosing spondylitis subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Back pain | 0 / 44 (0.00%) 0 0 / 44 (0.00%) 0 | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 44 (0.00%) | | |
| occurrences (all) | 0 | | |
| Bursitis | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | | |
| occurrences (all) | 1 | | |
| Foot deformity | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | | |
| occurrences (all) | 1 | | |
| Muscle contracture | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | | |
| occurrences (all) | 1 | | |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | | |
| occurrences (all) | 1 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | | |
| occurrences (all) | 0 | | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | | |
| occurrences (all) | 0 | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | | |
| occurrences (all) | 0 | | |
| Herpes simplex | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | | |
| occurrences (all) | 1 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 44 (4.55%) | | |
| occurrences (all) | 2 | | |
| Otitis externa | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | | |
| occurrences (all) | 1 | | |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|---|----------------|--|--|
| Rhinitis | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | | |
| occurrences (all) | 0 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 44 (0.00%) | | |
| occurrences (all) | 0 | | |
| Viral pharyngitis | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | | |
| occurrences (all) | 1 | | |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | | |
| occurrences (all) | 1 | | |
| Metabolism and nutrition disorders | | | |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | | |
| occurrences (all) | 1 | | |
| Lactose intolerance | | | |
| subjects affected / exposed | 1 / 44 (2.27%) | | |
| occurrences (all) | 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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.

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|---|
| Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.nov for complete trial results. |
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Notes: