



Clinical trial results:

A 52-week, multicenter study to assess the time course of response to secukinumab on joint inflammation using Power Doppler ultrasonography in patients with active psoriatic arthritis.

Summary

| | |
|--------------------------|-------------------------------------|
| EudraCT number | 2015-002394-38 |
| Trial protocol | GB IE ES HU BE NO FR AT NL CZ DE IT |
| Global end of trial date | 10 November 2020 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 25 November 2021 |
| First version publication date | 25 November 2021 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | CAIN457F2354 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02662985 |
| 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 | Study Director, Novartis Pharma AG, 1 8627788300, 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 | 10 November 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 10 November 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that there is a difference between secukinumab and placebo in terms of joint synovitis response over 12 weeks as measured by the PDUS Global EULAR-OMERACT-Synovitis Score (GLOESS) of the affected joints (out of 48 joints) in PsA patients with an inadequate response to non-biologic DMARDs.

Protection of trial subjects:

This 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 | 22 August 2016 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Argentina: 18 |
| Country: Number of subjects enrolled | Austria: 4 |
| Country: Number of subjects enrolled | Belgium: 10 |
| Country: Number of subjects enrolled | Canada: 2 |
| Country: Number of subjects enrolled | Colombia: 1 |
| Country: Number of subjects enrolled | Czechia: 19 |
| Country: Number of subjects enrolled | France: 14 |
| Country: Number of subjects enrolled | Germany: 9 |
| Country: Number of subjects enrolled | Hungary: 8 |
| Country: Number of subjects enrolled | Ireland: 1 |
| Country: Number of subjects enrolled | Italy: 5 |
| Country: Number of subjects enrolled | Mexico: 49 |
| Country: Number of subjects enrolled | Netherlands: 2 |
| Country: Number of subjects enrolled | Norway: 2 |
| Country: Number of subjects enrolled | Spain: 15 |
| Country: Number of subjects enrolled | United Kingdom: 2 |
| Country: Number of subjects enrolled | United States: 5 |

| | |
|------------------------------------|-----|
| Worldwide total number of subjects | 166 |
| EEA total number of subjects | 89 |

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) | 155 |
| From 65 to 84 years | 11 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

166 participants enrolled in 17 countries

Pre-assignment

Screening details:

83 participants were randomized to each group

Period 1

| | |
|------------------------------|---|
| Period 1 title | Treatment Period 1 |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer |

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | Yes |
| Arm title | Group 1 - Secukinumab (150 mg + 300 mg) |

Arm description:

In Treatment Period-1: Patients in this group were administered secukinumab 150 or 300 mg according to the severity of skin PSO disease with 12 weeks of treatment from baseline. In Treatment Period-2: Patients continued to receive the same dose of secukinumab every 4 weeks until Week 24 (although primary outcome was to week 12 only) In Treatment Period 3 (extension period): the extension period allowed responder patients the possibility to continue open-label secukinumab treatment at the same previous dose up to Week 52

| | |
|--|------------------|
| Arm type | Experimental |
| Investigational medicinal product name | secukinumab |
| Investigational medicinal product code | AIN457 |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

150 mg and 300 mg s.c.

| | |
|------------------|-------------------|
| Arm title | Group 2 - Placebo |
|------------------|-------------------|

Arm description:

In Treatment Period-1: Patients received placebo at baseline and same time points as secukinumab until Week 8. In Treatment Period-2: Patients commenced open-label secukinumab 150 or 300 mg according to the severity of skin PSO disease 150 mg for mild PSO and 300 mg for moderate to severe PSO every 4 weeks from Week 12, as follows, based on their severity of skin disease at Week 12 In Treatment Period-3: Continue with the same dose of secukinumab 150 mg or 300 mg open-label

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

Dosage and administration details:

150 mg and 300 mg s.c.

| Number of subjects in period 1 | Group 1 - Secukinumab (150 mg + 300 mg) | Group 2 - Placebo |
|--------------------------------|---|-------------------|
| Started | 83 | 83 |
| Completed | 82 | 79 |
| Not completed | 1 | 4 |
| Physician decision | 1 | - |
| Consent withdrawn by subject | - | 1 |
| Adverse event, non-fatal | - | 2 |
| Protocol deviation | - | 1 |

Period 2

| | |
|------------------------------|---|
| Period 2 title | Treatment period 2 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer |

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | Yes |
| Arm title | Group 1 - Secukinumab (150 mg + 300 mg) |

Arm description:

In Treatment Period-1: Patients in this group were administered secukinumab 150 or 300 mg according to severity of skin disease with 12 weeks of treatment from baseline. In Treatment Period-2: Patients continued to receive the same active dose of secukinumab every 4 weeks until Week 24 (although primary outcome was to week 12 only) In Treatment Period 3 (extension period): the extension period allowed responder patients the possibility to continue open-label secukinumab treatment up to Week 52

| | |
|--|------------------|
| Arm type | Experimental |
| Investigational medicinal product name | secukinumab |
| Investigational medicinal product code | AIN457 |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

150 mg and 300 mg s.c.

| | |
|------------------|-------------------------------|
| Arm title | Group 2 - Placebo/secukinumab |
|------------------|-------------------------------|

Arm description:

In Treatment Period-1: Patients received placebo at baseline and same time points as secukinumab until Week 8. In Treatment Period-2: Patients commenced open-label secukinumab 150 or 300 mg every 4 weeks from Week 12, as follows, based on severity of skin psoriasis at Week 12 In Treatment Period-3: Continued with the same dose of secukinumab 150 mg or 300 mg open label.

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

Dosage and administration details:

150 mg and 300 mg s.c.

| Number of subjects in period 2 | Group 1 - Secukinumab (150 mg + 300 mg) | Group 2 - Placebo/secukinuma b |
|--------------------------------|---|--------------------------------------|
| Started | 82 | 79 |
| Completed | 81 | 78 |
| Not completed | 1 | 1 |
| Lost to follow-up | 1 | - |
| Lack of efficacy | - | 1 |

Period 3

| | |
|------------------------------|---|
| Period 3 title | Treatment period 3 (extension period) |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer |

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | Yes |
| Arm title | Group 1 - Secukinumab (150 mg + 300 mg) |

Arm description:

In Treatment Period-1: Patients in this group were administered secukinumab 150 or 300 mg according to the severity of skin disease with 12 weeks of treatment from baseline. In Treatment Period-2: Patients continued to receive the same active dose of secukinumab every 4 weeks until Week 24 (although primary outcome was to week 12 only) In Treatment Period 3 (extension period): the extension period allowed responder patients the possibility to continue open-label secukinumab treatment at the same dose up to Week 52

| | |
|--|------------------|
| Arm type | Experimental |
| Investigational medicinal product name | secukinumab |
| Investigational medicinal product code | AIN457 |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

150 mg and 300 mg s.c.

| | |
|-----------|-------------------------------|
| Arm title | Group 2 - Placebo/secukinumab |
|-----------|-------------------------------|

Arm description:

In Treatment Period-1: Patients received placebo at baseline and same time points as secukinumab until Week 8. In Treatment Period-2: Patients commenced open-label secukinumab 150 or 300 mg according to severity of skin PSO 150 mg for mild PSO and 300 mg for moderate to severe skin PSO every 4

weeks from Week 12, as follows, based on severity of skin psoriasis at Week 12 In Treatment Period-3:
Open-label secukinumab at the same dose continued to be assigned to patients

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

Dosage and administration details:

150 mg and 300 mg s.c.

| Number of subjects in period 3 | Group 1 - Secukinumab (150 mg + 300 mg) | Group 2 - Placebo/secukinuma b |
|---------------------------------------|---|--------------------------------------|
| Started | 81 | 78 |
| Completed | 75 | 69 |
| Not completed | 6 | 9 |
| Adverse event, serious fatal | - | 1 |
| Consent withdrawn by subject | 1 | 2 |
| Withdrew before entering period | 4 | 4 |
| Adverse event, non-fatal | 1 | 1 |
| Lack of efficacy | - | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | Group 1 - Secukinumab (150 mg + 300 mg) |
|-----------------------|---|

Reporting group description:

In Treatment Period-1: Patients in this group were administered secukinumab 150 or 300 mg according to the severity of skin PSO disease with 12 weeks of treatment from baseline. In Treatment Period-2: Patients continued to receive the same dose of secukinumab every 4 weeks until Week 24 (although primary outcome was to week 12 only) In Treatment Period 3 (extension period): the extension period allowed responder patients the possibility to continue open-label secukinumab treatment at the same previous dose up to Week 52

| | |
|-----------------------|-------------------|
| Reporting group title | Group 2 - Placebo |
|-----------------------|-------------------|

Reporting group description:

In Treatment Period-1: Patients received placebo at baseline and same time points as secukinumab until Week 8. In Treatment Period-2: Patients commenced open-label secukinumab 150 or 300 mg according to the severity of skin PSO disease 150 mg for mild PSO and 300 mg for moderate to severe PSO every 4 weeks from Week 12, as follows, based on their severity of skin disease at Week 12 In Treatment Period-3: Continue with the same dose of secukinumab 150 mg or 300 mg open-label

| Reporting group values | Group 1 - Secukinumab (150 mg + 300 mg) | Group 2 - Placebo | Total |
|---|---|-------------------|-------|
| Number of subjects | 83 | 83 | 166 |
| Age Categorical Units: | | | |
| <=18 years | 0 | 0 | 0 |
| Between 18 and 65 years | 76 | 79 | 155 |
| >=65 years | 7 | 4 | 11 |
| Age Continuous Units: years | | | |
| arithmetic mean | 46.7 | 46.7 | |
| standard deviation | ± 12.35 | ± 12.08 | - |
| Sex: Female, Male Units: | | | |
| Female | 45 | 46 | 91 |
| Male | 38 | 37 | 75 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Caucasian | 75 | 75 | 150 |
| Asian | 1 | 0 | 1 |
| Native American | 4 | 8 | 12 |
| Unknown | 2 | 0 | 2 |
| Other | 1 | 0 | 1 |

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | Group 1 - Secukinumab (150 mg + 300 mg) |
| Reporting group description: In Treatment Period-1: Patients in this group were administered secukinumab 150 or 300 mg according to the severity of skin PSO disease with 12 weeks of treatment from baseline. In Treatment Period-2: Patients continued to receive the same dose of secukinumab every 4 weeks until Week 24 (although primary outcome was to week 12 only) In Treatment Period 3 (extension period): the extension period allowed responder patients the possibility to continue open-label secukinumab treatment at the same previous dose up to Week 52 | |
| Reporting group title | Group 2 - Placebo |
| Reporting group description: In Treatment Period-1: Patients received placebo at baseline and same time points as secukinumab until Week 8. In Treatment Period-2: Patients commenced open-label secukinumab 150 or 300 mg according to the severity of skin PSO disease 150 mg for mild PSO and 300 mg for moderate to severe PSO every 4 weeks from Week 12, as follows, based on their severity of skin disease at Week 12 In Treatment Period-3: Continue with the same dose of secukinumab 150 mg or 300 mg open-label | |
| Reporting group title | Group 1 - Secukinumab (150 mg + 300 mg) |
| Reporting group description: In Treatment Period-1: Patients in this group were administered secukinumab 150 or 300 mg according to severity of skin disease with 12 weeks of treatment from baseline. In Treatment Period-2: Patients continued to receive the same active dose of secukinumab every 4 weeks until Week 24 (although primary outcome was to week 12 only) In Treatment Period 3 (extension period): the extension period allowed responder patients the possibility to continue open-label secukinumab treatment up to Week 52 | |
| Reporting group title | Group 2 - Placebo/secukinumab |
| Reporting group description: In Treatment Period-1: Patients received placebo at baseline and same time points as secukinumab until Week 8. In Treatment Period-2: Patients commenced open-label secukinumab 150 or 300 mg every 4 weeks from Week 12, as follows, based on severity of skin psoriasis at Week 12 In Treatment Period-3: Continued with the same dose of secukinumab 150 mg or 300 mg open label. | |
| Reporting group title | Group 1 - Secukinumab (150 mg + 300 mg) |
| Reporting group description: In Treatment Period-1: Patients in this group were administered secukinumab 150 or 300 mg according to the severity of skin disease with 12 weeks of treatment from baseline. In Treatment Period-2: Patients continued to receive the same active dose of secukinumab every 4 weeks until Week 24 (although primary outcome was to week 12 only) In Treatment Period 3 (extension period): the extension period allowed responder patients the possibility to continue open-label secukinumab treatment at the same dose up to Week 52 | |
| Reporting group title | Group 2 - Placebo/secukinumab |
| Reporting group description: In Treatment Period-1: Patients received placebo at baseline and same time points as secukinumab until Week 8. In Treatment Period-2: Patients commenced open-label secukinumab 150 or 300 mg according to severity of skin PSO 150 mg for mild PSO and 300 mg for moderate to severe skin PSO every 4 weeks from Week 12, as follows, based on severity of skin psoriasis at Week 12 In Treatment Period-3: Open-label secukinumab at the same dose continued to be assigned to patients | |

Primary: Difference between secukinumab and placebo in terms of joint synovitis as measured by the Power Doppler Ultrasonography (PDUS) Global OMERACT-EULAR Synovitis Score (GLOESS)

| | |
|--|--|
| End point title | Difference between secukinumab and placebo in terms of joint synovitis as measured by the Power Doppler Ultrasonography (PDUS) Global OMERACT-EULAR Synovitis Score (GLOESS) |
| End point description: Mixed model repeated measures (MMRM) analysis of change in Global OMERACT-EULAR Synovitis Score (GLOESS) score at Week 12 (observed data) to compare treatments. | |

GLOESS score can vary from 0 to 144 with highest rating reflecting higher severity.

| | |
|----------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| 12 weeks | |

| End point values | Group 1 - Secukinumab (150 mg + 300 mg) | Group 2 - Placebo | | |
|---------------------------------------|---|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 83 | 81 | | |
| Units: Adjusted Mean Change in scores | | | | |
| arithmetic mean (standard error) | -9.05 (\pm 0.94) | -5.86 (\pm 0.93) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | PDUS GLOESS score |
| Statistical analysis description: | |
| GLOESS scores | |
| Comparison groups | Group 2 - Placebo v Group 1 - Secukinumab (150 mg + 300 mg) |
| Number of subjects included in analysis | 164 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.004 |
| Method | Mixed models analysis |
| Parameter estimate | Adjusted Mean Difference |
| Point estimate | -3.18 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.52 |
| upper limit | -0.85 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.18 |

Secondary: Proportion of Participants with American College of Rheumatology (ACR)-20 response - Key Secondary

| | |
|---|--|
| End point title | Proportion of Participants with American College of Rheumatology (ACR)-20 response - Key Secondary |
| End point description: | |
| Key Secondary Outcome: ACR 20 responder has \geq 20% improvement in TJC and SJC and >20% improvement in 3 of the following 5 domains: patient's assessment of disease activity, physician's assessment of disease activity, patient's assessment of PsA pain, HAQ-DI, or hsCRP. | |
| End point type | Secondary |

End point timeframe:

Week 12

| End point values | Group 1 - Secukinumab (150 mg + 300 mg) | Group 2 - Placebo | | |
|-----------------------------|--|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 83 | 83 | | |
| Units: participants | 56 | 26 | | |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | ACR-20 |
| Statistical analysis description: | |
| Proportion of patients with ACR 20 response at Week 12 (FAS) | |
| Comparison groups | Group 1 - Secukinumab (150 mg + 300 mg) v Group 2 - Placebo |
| Number of subjects included in analysis | 166 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 4.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.38 |
| upper limit | 8.89 |

Secondary: Proportion of Participants with American College of Rheumatology (ACR)-50 response - Key Secondary

| | |
|--|--|
| End point title | Proportion of Participants with American College of Rheumatology (ACR)-50 response - Key Secondary |
| End point description: | |
| ACR 50 responder has $\geq 50\%$ improvement in TJC and SJC and $>25\%$ improvement in 3 of the following 5 domains: patient's assessment of disease activity, physician's assessment of disease activity, patient's assessment of PsA pain, HAQ-DI, or hsCRP. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 12 | |

| | | | | |
|-----------------------------|---|-------------------|--|--|
| End point values | Group 1 - Secukinumab (150 mg + 300 mg) | Group 2 - Placebo | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 83 | 83 | | |
| Units: participants | 38 | 7 | | |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | ACR-50 |
| Statistical analysis description: | |
| Proportion of patients with ACR 50 response at Week 12 (FAS) | |
| Comparison groups | Group 1 - Secukinumab (150 mg + 300 mg) v Group 2 - Placebo |
| Number of subjects included in analysis | 166 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 9.65 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.92 |
| upper limit | 23.75 |

Secondary: Spondyloarthritis Research Consortium of Canada (SPARCC) - Key Secondary

| | |
|--|--|
| End point title | Spondyloarthritis Research Consortium of Canada (SPARCC) - Key Secondary |
| End point description: | |
| Repeated measures mixed effect (MMRM) analysis of SPARCC total score change from baseline to Week 12 between the 2 treatment groups. | |
| SPARCC index ranges from 0 to 16. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to Week 12 | |

| End point values | Group 1 - Secukinumab (150 mg + 300 mg) | Group 2 - Placebo | | |
|---------------------------------------|--|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 83 | 81 | | |
| Units: Adjusted mean change in scores | | | | |
| arithmetic mean (standard error) | -2.23 (± 0.29) | -1.57 (± 0.29) | | |

Statistical analyses

| Statistical analysis title | SPARCC |
|--|---|
| Statistical analysis description: SPARCC total score change | |
| Comparison groups | Group 1 - Secukinumab (150 mg + 300 mg) v Group 2 - Placebo |
| Number of subjects included in analysis | 164 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0327 |
| Method | Mixed models analysis |
| Parameter estimate | Adjusted Mean Difference |
| Point estimate | -0.67 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.374 |
| upper limit | 0.043 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs and SAEs were collected for the maximum duration of treatment and follow up for a participant per protocol for 12 weeks. All cause mortality (deaths) was collected from FPFV to LPLV up to a maximum of 52 weeks

Adverse event reporting additional description:

Adverse Events (AEs) are any untoward sign or symptom that occurs during the study treatment period with a frequency greater than or equal to 2%

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 23.1 |

Reporting groups

| | |
|-----------------------|--------------------------|
| Reporting group title | Secukinumab (150+300 mg) |
|-----------------------|--------------------------|

Reporting group description:

Secukinumab (150+300 mg)

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

Reporting group description:

Placebo

| Serious adverse events | Secukinumab (150+300 mg) | Placebo | |
|---|-----------------------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 9 / 161 (5.59%) | 2 / 83 (2.41%) | |
| number of deaths (all causes) | 1 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Invasive ductal breast carcinoma | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 0 / 83 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ovarian cancer | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 0 / 83 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostate cancer | | | |

| | | | |
|---|-----------------|----------------|--|
| subjects affected / exposed | 1 / 161 (0.62%) | 0 / 83 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 83 (1.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Incisional hernia | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 0 / 83 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 2 / 161 (1.24%) | 0 / 83 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 0 / 83 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery stenosis | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 0 / 83 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 161 (0.00%) | 1 / 83 (1.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Ovarian cyst | | | |

| | | | |
|---|-----------------|----------------|--|
| subjects affected / exposed | 1 / 161 (0.62%) | 0 / 83 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine polyp | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 0 / 83 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| COVID-19 | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 0 / 83 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Malnutrition | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 0 / 83 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 2 %

| Non-serious adverse events | Secukinumab (150+300 mg) | Placebo | |
|---|-----------------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 79 / 161 (49.07%) | 27 / 83 (32.53%) | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 1 / 161 (0.62%) | 2 / 83 (2.41%) | |
| occurrences (all) | 1 | 3 | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 9 / 161 (5.59%) | 1 / 83 (1.20%) | |
| occurrences (all) | 11 | 1 | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 2 / 161 (1.24%) | 2 / 83 (2.41%) | |
| occurrences (all) | 2 | 2 | |

| | | | |
|---|--|--|--|
| Headache subjects affected / exposed occurrences (all) | 13 / 161 (8.07%) 18 | 3 / 83 (3.61%) 3 | |
| General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) | 4 / 161 (2.48%) 4 4 / 161 (2.48%) 4 | 1 / 83 (1.20%) 1 0 / 83 (0.00%) 0 | |
| Eye disorders Dry eye subjects affected / exposed occurrences (all) | 3 / 161 (1.86%) 3 | 3 / 83 (3.61%) 3 | |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) | 5 / 161 (3.11%) 5 4 / 161 (2.48%) 4 7 / 161 (4.35%) 9 4 / 161 (2.48%) 4 | 3 / 83 (3.61%) 3 1 / 83 (1.20%) 1 6 / 83 (7.23%) 6 1 / 83 (1.20%) 1 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Productive cough subjects affected / exposed occurrences (all) Rhinorrhoea | 9 / 161 (5.59%) 10 0 / 161 (0.00%) 0 | 2 / 83 (2.41%) 2 2 / 83 (2.41%) 2 | |

| | | | |
|--|----------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 2 / 161 (1.24%) 2 | 2 / 83 (2.41%) 2 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 3 / 161 (1.86%) | 3 / 83 (3.61%) | |
| occurrences (all) | 3 | 4 | |
| Back pain | | | |
| subjects affected / exposed | 4 / 161 (2.48%) | 2 / 83 (2.41%) | |
| occurrences (all) | 4 | 2 | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 8 / 161 (4.97%) | 2 / 83 (2.41%) | |
| occurrences (all) | 9 | 2 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 4 / 161 (2.48%) | 1 / 83 (1.20%) | |
| occurrences (all) | 4 | 1 | |
| Influenza | | | |
| subjects affected / exposed | 7 / 161 (4.35%) | 3 / 83 (3.61%) | |
| occurrences (all) | 7 | 4 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 19 / 161 (11.80%) | 4 / 83 (4.82%) | |
| occurrences (all) | 26 | 5 | |
| Oral herpes | | | |
| subjects affected / exposed | 4 / 161 (2.48%) | 1 / 83 (1.20%) | |
| occurrences (all) | 6 | 1 | |
| Pharyngitis | | | |
| subjects affected / exposed | 5 / 161 (3.11%) | 0 / 83 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 4 / 161 (2.48%) | 2 / 83 (2.41%) | |
| occurrences (all) | 4 | 2 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 10 / 161 (6.21%) | 3 / 83 (3.61%) | |
| occurrences (all) | 10 | 3 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|--|
| 09 June 2016 | <p>For those countries where it was required, hepatitis B, hepatitis C and human immunodeficiency virus (HIV) serology testing during the Screening Period were added to the assessment schedule. These tests were already outlined in Exclusion Criterion No. 21 and results of these tests determined eligibility for the study. Thus the addition to the assessment schedule in this amendment was made in order to clarify and remove inconsistencies in the protocol.</p> <p>Collection of SPARCC at the Screening Visit was added to the assessment schedule as it was previously omitted in error. This test was already outlined in Inclusion Criterion No.5 and results of this test determined eligibility for the study. Thus the addition to the assessment schedule in this amendment was made in order to clarify and remove inconsistencies in the protocol.</p> |
| 02 March 2017 | <p>1. To increase the study feasibility and to ease the study visit burden on patients without compromising the primary and secondary objectives of the study until Week 12.</p> <p>Inclusion criterion no. 4, an ultrasound entry criterion that was considered too restrictive as it resulted in the most screen failures, was amended to allow inclusion of patients with a total synovitis score ≥ 2 and inflammation related to PD signal ≥ 2 for at least 1 affected joint as observed via PDUS of 48 joints, OR with an inflammation related to PD signal ≥ 1 for at least 2 affected joints as observed via PDUS of 48 joints.</p> <p>The study visits and associated study assessments at Week 28, 32, 40, 44 and 48 were removed from the open-label Extension Period and home administration of study drug was introduced at these time points. The clinical efficacy assessments (including PDUS assessments) were removed from the double-blind Week 3 visit; and the PDUS assessment was removed from the Week 56 follow-up visit. The Extension Period was optional according to Investigator's judgment and patient consent and exploratory study objectives only applied to this period. The removal of study visits during the Extension Period did not compromise patient safety given the benefit/ risk of secukinumab had already been assessed and secukinumab was registered in all participating countries.</p> <p>2. Different aspects of the protocol were clarified following the review of different Ethics Committees (ECs):</p> <p>Clarification was made in the patient population that patients must have had an inadequate response to non-biologic DMARDs to be consistent with study rationale and primary objective of the study.</p> <p>The use of rescue medication was amended so it was less restrictive throughout the study and to make it more ethical for the patients randomized to placebo during the first 12 weeks given the risk of potential flare and existence of alternative therapies.</p> |

| | |
|------------------|---|
| 27 November 2018 | <p>The sample size calculation in the trial was updated keeping in mind the difficulties of recruitment. The initial sample size calculation for this trial was extrapolated from an ultrasound study assessed to evaluate the early response of abatacept on synovitis in patients with rheumatoid arthritis (D'Agostino et al 2016a) given the lack of a previous ultrasound PsA trial with biologics. A blinded sample size re-estimation was supplemented with data from the first 72 patients who reached their Week 12 visit to provide the most accurate estimation. The sample size was adjusted to a new target of 164 patients in total (82 patients per arm). This was the mid-way point of the range plus a 5% adjustment based on the dropout rate of patients prior to Week 12 observed at the time of this calculation. The reduction of sample size from 218 to 164 patients helped achieve completion of the last patient first visit by the end of August 2019.</p> <p>2. Different aspects of the protocol were clarified following comments from the Health Authorities (HA), Ethics Committees and investigators.</p> <p>a. The dose of non-steroidal anti-inflammatory drugs (NSAIDs) as rescue therapy prior to assessments in the trial until Week 24 was clarified. The requirement for patients to return to their previous NSAIDs' dose following a transient increase in dose as rescue therapy 48 hours prior to study assessments was considered unethical by investigators and not accepted by patients who were in pain, and was therefore removed from the protocol.</p> |
|------------------|---|

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported