# Clinical trial results:
# A randomized, open label multicenter trial to investigate the efficacy of a treat-to-target treatment strategy with secukinumab (AIN457) as a first-line biologic compared to a standard-of-care treatment over 36 weeks in patients with active axial spondyloarthritis (axSpA) - AScalate

## Summary

| | |
|---|---|
| EudraCT number | 2018-003882-32 |
| Trial protocol | DE FR |
| Global end of trial date | 22 September 2022 |

**Results information**

| | |
|---|---|
| Result version number | v2 (current) |
| This version publication date | 21 June 2025 |
| First version publication date | 07 October 2023 |
| Version creation reason | |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | CAIN457HDE01 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03906136 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Novartis Pharma AG |
| Sponsor organisation address | Novartis Campus, 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 | 22 September 2022 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 22 September 2022 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To demonstrate that the efficacy of the T2T approach (with secukinumab as first-line biologic) is superior to the SOC approach based on the percentage of patients achieving an ASAS40 response at Week 24.

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 | 04 June 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 | France: 59 |
| Country: Number of subjects enrolled | Germany: 245 |
| Worldwide total number of subjects | 304 |
| EEA total number of subjects | 304 |

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) | 293 |
| From 65 to 84 years | 11 |

| | |
|---|---|
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

The study included an 8-week Screening period.

### Period 1

| | |
|---|---|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Treat-to-Target (T2T) |

Arm description:

Treat To Target approach with secukinumab as first line biologic

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

Dosage and administration details:

adalimumab biosimilar 40 mg

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

Dosage and administration details:

secukinumab 150 mg, secukinumab 300 mg

| | |
|---|---|
| **Arm title** | Standard-of-care (SOC) |

Arm description:

Patients received treatment according to local practice standards by their treating physician following the current treatment recommendations

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | treatment according to local practice standards by their treating physician following the current treatment recommendations. |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection/infusion in pre-filled syringe, Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

treatment according to local practice standards by their treating physician following the current treatment recommendations.

| **Number of subjects in period 1** | Treat-to-Target (T2T) | Standard-of-care (SOC) |
|---|---|---|
| Started | 155 | 149 |
| Completed | 143 | 138 |
| Not completed | 12 | 11 |
| Physician decision | 1 | - |
| Consent withdrawn by subject | 3 | 7 |
| Adverse event, non-fatal | 1 | - |
| Lost to follow-up | 7 | 4 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Treat-to-Target (T2T) |
| Reporting group description: | |
| Treat To Target approach with secukinumab as first line biologic | |
| Reporting group title | Standard-of-care (SOC) |
| Reporting group description: | |
| Patients received treatment according to local practice standards by their treating physician following the current treatment recommendations | |

| Reporting group values | Treat-to-Target (T2T) | Standard-of-care (SOC) | Total |
|---|---|---|---|
| Number of subjects | 155 | 149 | 304 |
| Age Categorical<br>Units: Participants | | | |
| <=18 years | 0 | 0 | 0 |
| Between 18 and 65 years | 149 | 144 | 293 |
| >=65 years | 6 | 5 | 11 |
| Age Continuous<br>Units: Years | | | |
| arithmetic mean | 40.0 | 38.6 | |
| standard deviation | ± 12.03 | ± 12.17 | - |
| Sex: Female, Male<br>Units: Participants | | | |
| Female | 59 | 51 | 110 |
| Male | 96 | 98 | 194 |
| Race/Ethnicity, Customized<br>Units: Subjects | | | |
| Asian | 1 | 0 | 1 |
| Black or African American | 0 | 1 | 1 |
| White | 128 | 114 | 242 |
| More than one race | 0 | 1 | 1 |
| Other | 26 | 33 | 59 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Treat-to-Target (T2T) |
| Reporting group description: | |
| Treat To Target approach with secukinumab as first line biologic | |
| Reporting group title | Standard-of-care (SOC) |
| Reporting group description: | |
| Patients received treatment according to local practice standards by their treating physician following the current treatment recommendations | |

### Primary: Percentage of patients achieving an ASAS40 response at Week 24

| | |
|---|---|
| End point title | Percentage of patients achieving an ASAS40 response at Week 24 |
| End point description: | |
| Assessment of SpondyloArthritis International Society criteria (ASAS) consists of 4 domains measured on visual analog scales (VAS): 1. Patient's global assessment; 2. Patient's assessment of back pain; 3. Function represented by Bath Ankylosing Spondylitis Functional Index (BASFI) average of 10 questions; 4. Inflammation represented by mean duration and severity of morning stiffness, on the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). ASAS40 response is defined as an improvement of ≥40% and ≥2 units on a scale of 0 - 10 in at least three of the four ASAS domains and no worsening at all in the remaining domain. A score of 0 indicates less severity; a score of 10 indicates more severity. Percentage was calculated from a logistic regression model: logit(proportion) = treatment + baseline quick C-reactive protein (CRP) + baseline weight. | |
| End point type | Primary |
| End point timeframe: | |
| Baseline, Week 24 | |

| End point values | Treat-to-Target (T2T) | Standard-of-care (SOC) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 144 | 139 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 40.1 | 49.2 | | |

### Statistical analyses

| | |
|---|---|
| **Statistical analysis title** | Comparison of T2T versus SOC |
| Statistical analysis description: | |
| Week 24 | |
| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |

| | |
|---|---|
| Number of subjects included in analysis | 283 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.119 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.69 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.43 |
| upper limit | 1.1 |

## Secondary: Percentage of patients achieving an ASAS40 response at Week 12

| | |
|---|---|
| End point title | Percentage of patients achieving an ASAS40 response at Week 12 |

End point description:

Assessment of SpondyloArthritis International Society criteria (ASAS) consists of 4 domains measured on visual analog scales (VAS): 1. Patient's global assessment; 2. Patient's assessment of back pain; 3. Function represented by Bath Ankylosing Spondylitis Functional Index (BASFI) average of 10 questions; 4. Inflammation represented by mean duration and severity of morning stiffness, on the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). ASAS40 response is defined as an improvement of ≥40% and ≥2 units on a scale of 0 - 10 in at least three of the four ASAS domains and no worsening at all in the remaining domain. A score of 0 indicates less severity; a score of 10 indicates more severity. Percentage was calculated from a logistic regression model: logit(proportion) = treatment + baseline quick C-reactive protein (CRP) + baseline weight.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Baseline, Week 12

| End point values | Treat-to-Target (T2T) | Standard-of-care (SOC) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 147 | 143 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 34.0 | 46.6 | | |

### Statistical analyses

| Statistical analysis title | Comparison of T2T versus SOC |
|---|---|

Statistical analysis description:

Week 12

| | |
|---|---|
| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |

| | |
|---|---|
| Number of subjects included in analysis | 290 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.029 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.59 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.37 |
| upper limit | 0.95 |

## Secondary: Percentage of patients achieving ASAS20 response

| | |
|---|---|
| End point title | Percentage of patients achieving ASAS20 response |

End point description:

Assessment of SpondyloArthritis International Society criteria (ASAS) consist of 4 domains measured on visual analog scales (VAS): 1. Patient's global assessment; 2. Patient's assessment of back pain; 3. Function represented by Bath Ankylosing Spondylitis Functional Index (BASFI) average of 10 questions; 4. Inflammation represented by mean duration and severity of morning stiffness, on the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). ASAS20 response is defined as an improvement of ≥20% and ≥1 unit on a scale of 0 - 10 in at least three of the four ASAS domains and no worsening at all in the remaining domain. A score of 0 indicates less severity; a score of 10 indicates more severity. Percentage was calculated from a logistic regression model: logit(proportion) = treatment + baseline quick C-reactive protein (CRP) + baseline weight.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Baseline, Weeks 12 and 24

| **End point values** | Treat-to-Target (T2T) | Standard-of-care (SOC) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 147 | 143 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 12 n=147,143 | 51.8 | 60.1 | | |
| Week 24 n=144,139 | 62.1 | 65.3 | | |

## Statistical analyses

| **Statistical analysis title** | Comparison of T2T versus SOC |
|---|---|

Statistical analysis description:

Week 24

| | |
|---|---|
| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |

| | |
|---|---|
| Number of subjects included in analysis | 290 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.562 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.87 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.54 |
| upper limit | 1.39 |

| **Statistical analysis title** | Comparison of T2T versus SOC |
|---|---|
| Statistical analysis description: | |
| Week 12 | |
| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |
| Number of subjects included in analysis | 290 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.154 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.71 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.45 |
| upper limit | 1.14 |

## Secondary: Percentage of patients achieving ASAS partial remission

| End point title | Percentage of patients achieving ASAS partial remission |
|---|---|

End point description:

Assessment of SpondyloArthritis International Society criteria (ASAS): 6 domains (4 main; 2 additional assessment domains): 1. Patient's global assessment measured on a visual analog scale (VAS); 2. Patient's assessment of back pain, measured on a VAS; 3. Function represented by Bath Ankylosing Spondylitis Functional Index (BASFI) average of 10 questions as measured by VAS; 4. Inflammation represented by mean duration and severity of morning stiffness, on the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) as measured by VAS; 5. Spinal mobility represented by the Bath Ankylosing Spondylitis Metrology Index (BASMI) lateral spinal flexion assessment; 6. C-reactive protein (CRP, acute phase reactant).
ASAS partial remission: a value not above 2 units in each of the four main domains on a scale of 10. Higher score on VAS = higher severity. Percentage calculated from a logistic regression model: logit(proportion) = treatment + baseline quick CRP + baseline weight.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Weeks 12 and 24

| End point values | Treat-to-Target (T2T) | Standard-of-care (SOC) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 149 | 143 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 12 n=149, 143 | 18.2 | 29.0 | | |
| Week 24 n=146,139 | 22.8 | 28.5 | | |

**Statistical analyses**

| Statistical analysis title | Comparison of T2T versus SOC |
|---|---|
| Statistical analysis description: Week 24 | |
| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |
| Number of subjects included in analysis | 292 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.264 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.74 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.44 |
| upper limit | 1.25 |

| Statistical analysis title | Comparison of T2T versus SOC |
|---|---|
| Statistical analysis description: Week 12 | |
| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |
| Number of subjects included in analysis | 292 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.029 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.55 |

| Confidence interval | |
|---|---|
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.32 |
| upper limit | 0.94 |

## Secondary: Percentage of patients meeting the Ankylosing Spondylitis Disease Activity Score (ASDAS) definition of inactive disease

| End point title | Percentage of patients meeting the Ankylosing Spondylitis Disease Activity Score (ASDAS) definition of inactive disease |
|---|---|

End point description:

Parameters used for the ASDAS include spinal pain (Bath Ankylosing Spondylitis Disease Activity Index, BASDAI question 2), the patient's global assessment of disease activity, peripheral pain/swelling (BASDAI question 3), duration of morning stiffness (BASDAI question 6) and C-reactive Protein or Erythrocyte Sedimentation Rate).
The 3 values selected to separate disease activity states were < 1.3 between inactive disease and low disease activity, < 2.1 between low disease activity and high disease activity, and > 3.5 between high disease activity and very high disease activity. Selected cutoffs for improvement scores were a change of ≥ 1.1 unit for "minimal clinically important improvement" and a change of ≥ 2.0 units for "major improvement". Percentage was calculated from a logistic regression model: logit(proportion) = treatment + baseline ASDAS + baseline weight.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Weeks 12 and 24

| **End point values** | Treat-to-Target (T2T) | Standard-of-care (SOC) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 151 | 141 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 12 n=151,141 | 19.8 | 33.3 | | |
| Week 24 n=146,136 | 18.8 | 33.0 | | |

### Statistical analyses

| **Statistical analysis title** | Comparison of T2T versus SOC |
|---|---|

Statistical analysis description:

Week 24

| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |
|---|---|
| Number of subjects included in analysis | 292 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.005 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.47 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.28 |
| upper limit | 0.8 |

| **Statistical analysis title** | Comparison of T2T versus SOC |
|---|---|
| Statistical analysis description: | |
| Week 12 | |
| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |
| Number of subjects included in analysis | 292 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.008 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.49 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.29 |
| upper limit | 0.83 |

## Secondary: Percentage of patients with ASDAS major improvement

| End point title | Percentage of patients with ASDAS major improvement |
|---|---|

End point description:

Parameters used for the ASDAS include spinal pain (Bath Ankylosing Spondylitis Disease Activity Index, BASDAI question 2), the patient's global assessment of disease activity, peripheral pain/swelling (BASDAI question 3), duration of morning stiffness (BASDAI question 6) and C-reactive Protein or Erythrocyte Sedimentation Rate).
The 3 values selected to separate disease activity states were < 1.3 between inactive disease and low disease activity, < 2.1 between low disease activity and high disease activity, and > 3.5 between high disease activity and very high disease activity. Selected cutoffs for improvement scores were a change of ≥ 1.1 unit for "minimal clinically important improvement" and a change of ≥ 2.0 units for "major improvement". Percentage was calculated from a logistic regression model: logit(proportion) = treatment + baseline ASDAS + baseline weight.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Weeks 12 and 24

| End point values | Treat-to-Target (T2T) | Standard-of-care (SOC) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 151 | 141 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 12 n=151,141 | 19.8 | 25.6 | | |
| Week 24 n=146,136 | 18.6 | 27.1 | | |

## Statistical analyses

| Statistical analysis title | Comparison of T2T versus SOC |
|---|---|
| Statistical analysis description: Week 24 | |
| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |
| Number of subjects included in analysis | 292 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.103 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.61 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.34 |
| upper limit | 1.1 |

| Statistical analysis title | Comparison of T2T versus SOC |
|---|---|
| Statistical analysis description: Week 12 | |
| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |
| Number of subjects included in analysis | 292 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.263 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.72 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.4 |
| upper limit | 1.28 |

## Secondary: Percentage of patients with ASDAS low disease activity

| End point title | Percentage of patients with ASDAS low disease activity |
|---|---|

End point description:

Parameters used for the ASDAS include spinal pain (Bath Ankylosing Spondylitis Disease Activity Index, BASDAI question 2), the patient's global assessment of disease activity, peripheral pain/swelling (BASDAI question 3), duration of morning stiffness (BASDAI question 6) and C-reactive Protein or Erythrocyte Sedimentation Rate).
The 3 values selected to separate disease activity states were < 1.3 between inactive disease and low disease activity, < 2.1 between low disease activity and high disease activity, and > 3.5 between high disease activity and very high disease activity. Selected cutoffs for improvement scores were a change of ≥ 1.1 unit for "minimal clinically important improvement" and a change of ≥ 2.0 units for "major improvement". Percentage was calculated from a logistic regression model: logit(proportion) = treatment + baseline ASDAS + baseline weight.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Weeks 12 and 24

| **End point values** | Treat-to-Target (T2T) | Standard-of-care (SOC) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 151 | 141 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 12 n=151,141 | 46.5 | 57.7 | | |
| Week 24 n=146,136 | 52.4 | 57.2 | | |

### Statistical analyses

| **Statistical analysis title** | Comparison of T2T versus SOC |
|---|---|

Statistical analysis description:

Week 24

| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |
|---|---|
| Number of subjects included in analysis | 292 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.409 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.82 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.52 |
| upper limit | 1.31 |

| **Statistical analysis title** | Comparison of T2T versus SOC |
|---|---|

| | |
|---|---|
| Statistical analysis description: | |
| Week 12 | |
| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |
| Number of subjects included in analysis | 292 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.055 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.64 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.4 |
| upper limit | 1.01 |

## Secondary: Percentage of patients achieving the Bath Ankylosing Spondylitis Disease Activity Index response 50% (BASDAI 50) at Week 12 and Week 24

| | |
|---|---|
| End point title | Percentage of patients achieving the Bath Ankylosing Spondylitis Disease Activity Index response 50% (BASDAI 50) at Week 12 and Week 24 |

End point description:

The BASDAI consists of a 0 through 10 scale (0 being no problem and 10 being the worst problem, captured as a continuous VAS), which is used to answer 6 questions pertaining to the 5 major symptoms of the disease. BASDAI 50 response is defined as at least 50% improvement (decrease) in total BASDAI score.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Baseline, Weeks 12 and 24

| **End point values** | Treat-to-Target (T2T) | Standard-of-care (SOC) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 155 | 149 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 12 | 38.0 | 42.0 | | |
| Week 24 | 42.5 | 42.2 | | |

### Statistical analyses

| | |
|---|---|
| **Statistical analysis title** | Comparison of T2T versus SOC |
| Statistical analysis description: | |
| Week 24 | |
| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |

| | |
|---|---|
| Number of subjects included in analysis | 304 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.968 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.63 |
| upper limit | 1.61 |

| **Statistical analysis title** | Comparison of T2T versus SOC |
|---|---|
| Statistical analysis description: | |
| Week 12 | |
| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |
| Number of subjects included in analysis | 304 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.477 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.85 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.53 |
| upper limit | 1.34 |

## Secondary: Change from Baseline in Bath Ankylosing Spondylitis Functional Index (BASFI)

| End point title | Change from Baseline in Bath Ankylosing Spondylitis Functional Index (BASFI) |
|---|---|

End point description:

The Bath Ankylosing Spondylitis Functional Index (BASFI) is a set of 10 questions designed to determine the degree of functional limitation in those patients with AS. The 10 questions were chosen with major input from patients with AS. The first 8 questions consider activities related to functional anatomy. The final 2 questions assess the patients' ability to cope with everyday life. A 0 through 10 scale (captured as a continuous VAS) is used to answer the questions. The mean of the 10 scales gives the BASFI score – a value between 0 and 10. A higher score on the VAS signifies higher severity.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Weeks 12 and 24

| End point values | Treat-to-Target (T2T) | Standard-of-care (SOC) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 155 | 149 | | |
| Units: Scores on a scale | | | | |
| least squares mean (confidence interval 95%) | | | | |
| Week 12 | -1.69 (-2.01 to -1.37) | -1.99 (-2.31 to 1.66) | | |
| Week 24 | -1.97 (-2.28 to 1.65) | -2.33 (-2.66 to 2.01) | | |

**Statistical analyses**

| Statistical analysis title | Comparison of T2T versus SOC |
|---|---|
| Statistical analysis description: Week 24 | |
| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |
| Number of subjects included in analysis | 304 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.108 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.37 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.08 |
| upper limit | 0.82 |

| Statistical analysis title | Comparison of T2T versus SOC |
|---|---|
| Statistical analysis description: Week 12 | |
| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |
| Number of subjects included in analysis | 304 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.205 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.16 |
| upper limit | 0.75 |

## Secondary: Change from Baseline in Bath ankylosing spondylitis metrology index (BASMI)

| End point title | Change from Baseline in Bath ankylosing spondylitis metrology index (BASMI) |
|---|---|

End point description:

BASMI measures the range of motion based on five clinical measurements: 1) cervical rotation, 2) tragus to wall distance, 3) lumbar side flexion, 4) lumbar flexion (modified Schober's) and 5) intermalleolar distance. BASMI 0 = indicates mild disease involvement, 1 = moderate disease, and 2 = severe disease involvement. The results for cervical rotation and lumbar side flexion are the means of the left and right measurements. Scoring range 0-10. The higher the BASMI score, the more severe was the subject's limitation of movement.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Weeks 12 and 24

| **End point values** | Treat-to-Target (T2T) | Standard-of-care (SOC) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 155 | 149 | | |
| Units: Scores on a scale | | | | |
| least squares mean (confidence interval 95%) | | | | |
| Week 12 | -0.32 (-0.44 to -0.20) | -0.38 (-0.50 to -0.27) | | |
| Week 24 | -0.41 (-0.55 to -0.27) | -0.35 (-0.50 to -0.21) | | |

### Statistical analyses

| **Statistical analysis title** | Comparison of T2T versus SOC |
|---|---|

Statistical analysis description:

Week 24

| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |
|---|---|
| Number of subjects included in analysis | 304 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.577 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | -0.06 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.25 |
| upper limit | 0.14 |

| **Statistical analysis title** | Comparison of T2T versus SOC |
|---|---|
| Statistical analysis description:<br>Week 12 | |
| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |
| Number of subjects included in analysis | 304 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.525 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | 0.06 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.12 |
| upper limit | 0.23 |

| **Secondary: Change from Baseline in chest expansion** | |
|---|---|
| End point title | Change from Baseline in chest expansion |
| End point description:<br>Chest expansion is measured as the cervical rotation angle (in degrees). | |
| End point type | Secondary |
| End point timeframe:<br>Baseline, Weeks 12 and 24 | |

| **End point values** | Treat-to-Target (T2T) | Standard-of-care (SOC) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 155 | 149 | | |
| Units: degrees | | | | |
| least squares mean (confidence interval 95%) | | | | |
| Week 12 | 0.46 (-0.54 to 1.46) | 1.35 (0.33 to 2.38) | | |
| Week 24 | 0.47 (0.05 to 0.88) | 0.57 (0.14 to 1.00) | | |

**Statistical analyses**

| **Statistical analysis title** | Comparison of T2T versus SOC |
|---|---|

| Statistical analysis description: | |
|---|---|
| Week 12 | |
| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |
| Number of subjects included in analysis | 304 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.22 |
| Method | Mixed models analysis |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | -0.89 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.32 |
| upper limit | 0.54 |

| **Statistical analysis title** | Comparison of T2T versus SOC |
|---|---|
| Statistical analysis description: | |
| Week 24 | |
| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |
| Number of subjects included in analysis | 304 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.745 |
| Method | Regression, Logistic |
| Parameter estimate | Median difference (net) |
| Point estimate | -0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.7 |
| upper limit | 0.5 |

## Secondary: Change from Baseline in the ASQoL (Ankylosing Spondylitis Quality of Life instrument)

| End point title | Change from Baseline in the ASQoL (Ankylosing Spondylitis Quality of Life instrument) |
|---|---|

End point description:

The Ankylosing Spondylitis Quality of Life scores (ASQoL) is a self-administered questionnaire designed to assess health-related quality of life in adult patients with Ankylosing Spondylitis. The ASQoL contains 18 items with a dichotomous yes/no response option. A single point is assigned for each "yes" response and no points for each "no" response resulting in overall scores that range from 0 (least severity) to 18 (highest severity). As such, lower score indicate better quality of life. Items include an assessment of mobility/energy, self-care and mood/emotion. The recall period is "at the moment," and the measure requires approximately 6 minutes to complete.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Weeks 12 and 24

| End point values | Treat-to-Target (T2T) | Standard-of-care (SOC) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 155 | 149 | | |
| Units: Scores on a scale | | | | |
| least squares mean (confidence interval 95%) | | | | |
| Week 12 | -3.52 (-4.13 to 2.91) | -3.39 (-4.02 to 2.76) | | |
| Week 24 | -4.21 (-4.88 to 3.53) | -3.84 (-4.53 to 3.15) | | |

**Statistical analyses**

| Statistical analysis title | Comparison of T2T versus SOC |
|---|---|
| Statistical analysis description: Week 24 | |
| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |
| Number of subjects included in analysis | 304 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.451 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | -0.37 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.34 |
| upper limit | 0.6 |

| Statistical analysis title | Comparison of T2T versus SOC |
|---|---|
| Statistical analysis description: Week 12 | |
| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |
| Number of subjects included in analysis | 304 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.768 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | -0.13 |

| Confidence interval | |
|---|---|
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.01 |
| upper limit | 0.74 |

## Secondary: Change from Baseline in ASAS-HI (Ankylosing Spondyloarthritis International Society Health Index)

| End point title | Change from Baseline in ASAS-HI (Ankylosing Spondyloarthritis International Society Health Index) |
|---|---|

End point description:

The ASAS-HI is a disease-specific questionnaire that was developed based on the comprehensive International Classification of Functioning, Disability and Health Core Set (also known as the ICF Core Set) for AS. The ASAS HI is a linear composite measure and contains 17 items (dichotomous response option: "I agree" and "I do not agree"), which cover most of the ICF Core Set. The ASAS HI contains items addressing categories of pain, emotional functions, sleep, sexual function, mobility, self-care, and community life. The total sum of the ASAS HI ranges from 0 to 17, with a lower score indicating a better health status. In addition, the Environmental Factor (EF) Item Set contains items addressing categories of support/relationships, attitudes and health services. The EF Item Set contains 9 dichotomous items with an identical response option but without a sum score because of its multidimensional nature.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Weeks 12 and 24

| End point values | Treat-to-Target (T2T) | Standard-of-care (SOC) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 155 | 149 | | |
| Units: Scores on a scale | | | | |
| least squares mean (confidence interval 95%) | | | | |
| Week 12 | -2.55 (-3.05 to 2.05) | -2.81 (-3.32 to 2.30) | | |
| Week 24 | -3.24 (-3.77 to 2.72) | -3.07 (-3.61 to 2.54) | | |

### Statistical analyses

| Statistical analysis title | Comparison of T2T versus SOC |
|---|---|

Statistical analysis description:

Week 24

| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |
|---|---|

| | |
|---|---|
| Number of subjects included in analysis | 304 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.66 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | -0.17 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.92 |
| upper limit | 0.58 |

| **Statistical analysis title** | Comparison of T2T versus SOC |
|---|---|
| Statistical analysis description: | |
| Week 12 | |
| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |
| Number of subjects included in analysis | 304 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.477 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | 0.26 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.46 |
| upper limit | 0.97 |

## Secondary: Change from Baseline in global disease assessment (patient)

| End point title | Change from Baseline in global disease assessment (patient) |
|---|---|
| End point description: | |
| The patient’s global assessment of disease activity was performed using a 100 mm (visual analog scale) VAS, ranging from not severe (0 mm) to very severe (100 mm), in response to the question, "How active was your disease on average during the last week?” A higher score indicates more disease activity. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Weeks 12 and 24 | |

| End point values | Treat-to-Target (T2T) | Standard-of-care (SOC) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 155 | 149 | | |
| Units: Scores on a scale | | | | |
| least squares mean (confidence interval 95%) | | | | |
| Week 12 | -2.95 (-3.38 to 2.52) | -3.12 (-3.56 to 2.68) | | |
| Week 24 | -3.27 (-3.69 to 2.85) | -3.48 (-3.92 to 3.05) | | |

**Statistical analyses**

| Statistical analysis title | Comparison of T2T versus SOC |
|---|---|
| Statistical analysis description: Week 24 | |
| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |
| Number of subjects included in analysis | 304 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.491 |
| Method | Mixed models analysis |
| Parameter estimate | Median difference (net) |
| Point estimate | 0.21 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.39 |
| upper limit | 0.82 |

| Statistical analysis title | Comparison of T2T versus SOC |
|---|---|
| Statistical analysis description: Week 12 | |
| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |
| Number of subjects included in analysis | 304 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.586 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | 0.17 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.45 |
| upper limit | 0.79 |

## Secondary: Change from Baseline in global disease assessment (physician)

| End point title | Change from Baseline in global disease assessment (physician) |
|---|---|

End point description:

The physician's global assessment of disease activity was performed using a 100 mm VAS, ranging from not severe (0 mm) to very severe (100 mm), in response to the question, "Considering all the ways the disease affects your patient, draw a line on the scale for how well his or her condition is today." To enhance objectivity, the physician must not be aware of the specific patient's global assessment of disease activity when performing his own assessment on that patient. A higher score indicates more disease activity.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline, Weeks 12 and 24

| End point values | Treat-to-Target (T2T) | Standard-of-care (SOC) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 155 | 149 | | |
| Units: Scores on a scale | | | | |
| least squares mean (confidence interval 90%) | | | | |
| Week 12 | -32.46 (-35.98 to 28.94) | -36.96 (-40.60 to 33.31) | | |
| Week 24 | -35.81 (-39.34 to 32.28) | -38.54 (-42.19 to 34.89) | | |

### Statistical analyses

| Statistical analysis title | Comparison of T2T versus SOC |
|---|---|

Statistical analysis description:

Week 24

| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |
|---|---|
| Number of subjects included in analysis | 304 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.292 |
| Method | Mixed models analysis |
| Parameter estimate | Median difference (net) |
| Point estimate | 2.73 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.35 |
| upper limit | 7.81 |

| **Statistical analysis title** | Comparison of T2T versus SOC |
|---|---|
| Comparison groups | Treat-to-Target (T2T) v Standard-of-care (SOC) |
| Number of subjects included in analysis | 304 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.082 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | 4.49 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.58 |
| upper limit | 9.56 |

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| Timeframe for AE | |
| Adverse event reporting additional description: | |
| AE additional description | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 25.1 |

| Reporting groups | |
|---|---|
| Reporting group title | Secukinumab 150 mg |
| Reporting group description: | |
| Secukinumab 150 mg | |
| Reporting group title | Secukinumab 300 mg |
| Reporting group description: | |
| Secukinumab 300 mg | |
| Reporting group title | Overall |
| Reporting group description: | |
| Overall | |
| Reporting group title | Other |
| Reporting group description: | |
| Other | |
| Reporting group title | Adalimumab 40 mg |
| Reporting group description: | |
| Adalimumab 40 mg | |

| Serious adverse events | Secukinumab 150 mg | Secukinumab 300 mg | Overall |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 10 / 190 (5.26%) | 4 / 92 (4.35%) | 16 / 303 (5.28%) |
| 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) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 1 / 190 (0.53%) | 1 / 92 (1.09%) | 1 / 303 (0.33%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fibroadenoma of breast | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 190 (0.00%) | 0 / 92 (0.00%) | 1 / 303 (0.33%) |
| 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 | | | |
| Radius fracture | | | |
| subjects affected / exposed | 0 / 190 (0.00%) | 0 / 92 (0.00%) | 1 / 303 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscle strain | | | |
| subjects affected / exposed | 1 / 190 (0.53%) | 0 / 92 (0.00%) | 1 / 303 (0.33%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Scapula fracture | | | |
| subjects affected / exposed | 0 / 190 (0.00%) | 0 / 92 (0.00%) | 1 / 303 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Tachycardia | | | |
| subjects affected / exposed | 1 / 190 (0.53%) | 0 / 92 (0.00%) | 1 / 303 (0.33%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery disease | | | |
| subjects affected / exposed | 1 / 190 (0.53%) | 1 / 92 (1.09%) | 1 / 303 (0.33%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 190 (0.53%) | 1 / 92 (1.09%) | 1 / 303 (0.33%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Sciatica | | | |
| subjects affected / exposed | 0 / 190 (0.00%) | 0 / 92 (0.00%) | 1 / 303 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 1 / 190 (0.53%) | 1 / 92 (1.09%) | 1 / 303 (0.33%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Immunisation reaction | | | |
| subjects affected / exposed | 1 / 190 (0.53%) | 0 / 92 (0.00%) | 1 / 303 (0.33%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Diarrhoea haemorrhagic | | | |
| subjects affected / exposed | 1 / 190 (0.53%) | 0 / 92 (0.00%) | 1 / 303 (0.33%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis atopic | | | |
| subjects affected / exposed | 0 / 190 (0.00%) | 0 / 92 (0.00%) | 1 / 303 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Ankylosing spondylitis | | | |
| subjects affected / exposed | 2 / 190 (1.05%) | 0 / 92 (0.00%) | 2 / 303 (0.66%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 190 (0.00%) | 0 / 92 (0.00%) | 1 / 303 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Other | Adalimumab 40 mg | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 8 / 128 (6.25%) | 5 / 116 (4.31%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |

| | | | |
|---|---|---|---|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fibroadenoma of breast | | | |
| subjects affected / exposed | 1 / 128 (0.78%) | 1 / 116 (0.86%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Radius fracture | | | |
| subjects affected / exposed | 1 / 128 (0.78%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscle strain | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Scapula fracture | | | |
| subjects affected / exposed | 1 / 128 (0.78%) | 1 / 116 (0.86%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina pectoris | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 128 (0.00%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Sciatica | | | |
| subjects affected / exposed | 1 / 128 (0.78%) | 1 / 116 (0.86%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Immunisation reaction | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 1 / 116 (0.86%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Diarrhoea haemorrhagic | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis atopic | | | |
| subjects affected / exposed | 1 / 128 (0.78%) | 0 / 116 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Ankylosing spondylitis | | | |
| subjects affected / exposed | 2 / 128 (1.56%) | 1 / 116 (0.86%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoarthritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 128 (0.78%) | 0 / 116 (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: 5 %

| **Non-serious adverse events** | Secukinumab 150 mg | Secukinumab 300 mg | Overall |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 69 / 190 (36.32%) | 38 / 92 (41.30%) | 98 / 303 (32.34%) |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 12 / 190 (6.32%) | 7 / 92 (7.61%) | 18 / 303 (5.94%) |
| occurrences (all) | 13 | 8 | 20 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 7 / 190 (3.68%) | 3 / 92 (3.26%) | 12 / 303 (3.96%) |
| occurrences (all) | 7 | 3 | 13 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 16 / 190 (8.42%) | 9 / 92 (9.78%) | 24 / 303 (7.92%) |
| occurrences (all) | 17 | 10 | 25 |
| Nausea | | | |
| subjects affected / exposed | 12 / 190 (6.32%) | 6 / 92 (6.52%) | 14 / 303 (4.62%) |
| occurrences (all) | 14 | 6 | 16 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 7 / 190 (3.68%) | 6 / 92 (6.52%) | 8 / 303 (2.64%) |
| occurrences (all) | 7 | 6 | 8 |
| Infections and infestations | | | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 10 / 190 (5.26%) | 3 / 92 (3.26%) | 10 / 303 (3.30%) |
| occurrences (all) | 12 | 3 | 12 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 10 / 190 (5.26%) | 6 / 92 (6.52%) | 12 / 303 (3.96%) |
| occurrences (all) | 12 | 8 | 14 |
| Nasopharyngitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 24 / 190 (12.63%) | 13 / 92 (14.13%) | 31 / 303 (10.23%) |
| occurrences (all) | 28 | 14 | 38 |

| **Non-serious adverse events** | Other | Adalimumab 40 mg | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 36 / 128 (28.13%) | 35 / 116 (30.17%) | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 6 / 128 (4.69%) | 7 / 116 (6.03%) | |
| occurrences (all) | 6 | 8 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 5 / 128 (3.91%) | 6 / 116 (5.17%) | |
| occurrences (all) | 6 | 6 | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 11 / 128 (8.59%) | 8 / 116 (6.90%) | |
| occurrences (all) | 11 | 9 | |
| Nausea | | | |
| subjects affected / exposed | 7 / 128 (5.47%) | 3 / 116 (2.59%) | |
| occurrences (all) | 8 | 3 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 128 (0.00%) | 3 / 116 (2.59%) | |
| occurrences (all) | 0 | 3 | |
| Infections and infestations | | | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 3 / 128 (2.34%) | 3 / 116 (2.59%) | |
| occurrences (all) | 3 | 3 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 3 / 128 (2.34%) | 6 / 116 (5.17%) | |
| occurrences (all) | 3 | 7 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 10 / 128 (7.81%) | 7 / 116 (6.03%) | |
| occurrences (all) | 14 | 8 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 10 February 2021 | The main purpose of this amendment was to remove the planned IA that became obsolete due to availability of secukinumab data that fully supported the assumptions for the initial sample size calculation. |
| 19 May 2021 | The main purpose of this amendment was to incorporate two novel components into the protocol: Patient pain diary and Companion app. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported