NOVARTIS

**Clinical Trial Results Website**

## Sponsor

Novartis Pharmaceuticals

## Generic Drug Name

Secukinumab

## Trial Indication(s)

Non-radiographic axial spondyloarthritis (nr-axSpA)

## Protocol Number

CAIN457H2315

## Protocol Title

A randomized, double-blind, placebo-controlled multicenter study of secukinumab 150 mg in patients with active nr-axSpA to evaluate the safety,tolerability and efficacy up to 2 yrs, followed by an opt phase of either 150 mg or 300 mg randomized dose escalation for up to another 2 yrs

## Clinical Trial Phase

Phase 3

## Phase of Drug Development

Phase III

## Study Start/End Dates

Study Start Date: April 2016 (Actual)
Primary Completion Date: July 2019 (Actual)
Study Completion Date: March 2021 (Actual)

## Study Design/Methodology

This was a randomized, double-blind, placebo-controlled study, consisting of a core phase (up to Week 104) and an extension phase (Week 104 to Week 208). Patients were randomized to one of three treatment groups in the core phase (secukinumab 150 mg Load, secukinumab 150 mg No Load, or placebo in a ratio of 1:1:1).

Starting at Week 104, all patients who finished the core phase according to the protocol were asked to continue in an optional extension phase consisting of a 16-week dose escalation treatment period and a continuous treatment period. The patients were assessed based on their ASAS20 response at Week 104 as Core Phase Responders (i.e., achieving ASAS20 at Week 104) or Core Phase Non-Responders (i.e., not achieving ASAS20 at Week 104).

At Week 104, all patients who finished the core phase according to the protocol were asked to continue in an optional, exploratiry extension phase. Patients who achieved ASAS20 response at Week 104 (Core Phase Responders) were randomized to.secukinumab 150 mg or 300 mg. Patients not achieving ASAS20 at Week 104 (Core Phase Non-Responders) were escalated to secukinumab 300 mg in an open-label manner.

## Centers

140 centers in 24 countries: United Kingdom(9), Germany(14), United States(18), Austria(2), France(8), Belgium(3), Bulgaria(3), Japan(6), Netherlands(3), Poland(6), Russia(8), Spain(15), Switzerland(2), Hungary(6), Czech Republic(6), Portugal(5), Norway(2), Italy(5), Sweden(3), Israel(4), Australia(5), Korea, Republic of(2), Turkey(1), Mexico(4)

## Objectives:

There are two primary objectives based on regional regulatory precedent and feedback. These objectives will be tested in separate analysis plans.

Analysis Plan – European Union (EU) and other non-United States of America (USA) Regions

To demonstrate superiority of secukinumab 150 mg s.c. with loading over placebo at Week 16, based on the proportion of TNF naïve patients achieving an ASAS40 response (Assessment of SpondyloArthritis International Society criteria).

Analysis plan B - USA

To demonstrate superiority of secukinumab 150 mg s.c. without loading over placebo at Week 52, based on the proportion of TNF naïve patients achieving an ASAS40 response (Assessment of SpondyloArthritis International Society criteria)

The secondary objectives are as follows:

Analysis Plan A

1. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 16 is superior to placebo based on the proportion of all patients achieving an ASAS40 response
2. To demonstrate that the efficacy of secukinumab 150 mg s.c., without loading, at Week 16 is superior to placebo based on the proportion of TNF naïve patients achieving an ASAS40 response
3. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 16 is superior to placebo based on the proportion of patients meeting the ASAS 5/6 response criteria
4. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 16 is superior to placebo based on the change from baseline in total Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)
5. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 16 is superior to placebo based on the proportion of patients achieving BASDAI 50
6. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 16 is superior to placebo based on the change from baseline of high sensitivity C-Reactive Protein (hsCRP)
7. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 16 is superior to placebo based on the change from baseline in total Bath Ankylosing Spondylitis Functional Index (BASFI)
8. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 16 is superior to placebo based on the change from screening in SI joint edema on MRI
9. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 16 is superior to placebo based on the proportion of subjects achieving an ASAS20 response
10. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 16 is superior to placebo based on the change from baseline in Short Form-36 Physical Component Summary (SF-36 PCS)
11. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 16 is superior to placebo based on the change from baseline in Ankylosing Spondylitis Quality of Life (ASQoL) scores

12. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 16 is superior to placebo based on the proportion of patients achieving ASAS partial remission
13. Overall safety and tolerability of secukinumab

Analysis Plan B

1. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 52 is superior to placebo based on the proportion of all patients achieving an ASAS40 response
2. To demonstrate that the efficacy of secukinumab 150 mg s.c., with loading, at Week 52 is superior to placebo based on the proportion of TNF naïve patients achieving an ASAS40 response
3. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 16 is superior to placebo based on the proportion of subjects achieving an ASAS40 response
4. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 16 is superior to placebo based on the change from baseline in total Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)
5. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 16 is superior to placebo based on the proportion of patients achieving BASDAI 50
6. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 52 is superior to placebo based on the proportion of patients achieving BASDAI 50
7. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 16 is superior to placebo based on the change from baseline of high sensitivity C-Reactive Protein (hsCRP)
8. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 16 is superior to placebo based on the change from baseline in Short Form-36 Physical Component Summary (SF-36 PCS)
9. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 16 is superior to placebo based on the change from baseline in Ankylosing Spondylitis Quality of Life (ASQoL) scores
10. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 16 is superior to placebo based on the proportion of patients meeting the ASAS 5/6 response criteria
11. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 16 is superior to placebo based on the proportion of subjects achieving an ASAS20 response
12. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 16 is superior to placebo based on the change from baseline in total Bath Ankylosing Spondylitis Functional Index (BASFI)

13. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 16 is superior to placebo based on the change from screening in SI joint edema on MRI
14. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 52 is superior to placebo based on the proportion of patients achieving Ankylosing Spondylitis Disease Activity Score (ASDAS)-C-Reactive Protein (CRP) inactive disease as defined by ASDAS < 1.3
15. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 52 is superior to placebo based on the change from screening in SI joint edema on MRI
16. To demonstrate that the efficacy of secukinumab 150 mg s.c., with or without loading, at Week 52 is superior to placebo based on the change from baseline in Ankylosing Spondylitis Quality of Life (ASQoL) scores
17. Overall safety and tolerability of secukinumab

## Test Product (s), Dose(s), and Mode(s) of Administration

Patients were assigned to one of the following 3 treatment arms in a 1:1:1 ratio for the core phase up to Week 52. After Week 52, all patients received open-label secukinumab 150 mg s.c. unless they had discontinued study treatment.

- Secukinumab 150 mg Load
- Secukinumab 150 mg No Load
- Placebo

After the core phase of the study, patients could join the extension phase and received either blinded or open-label treatment consisting of two injections per treatment.

Patients in the extension phase were assigned to one of the following three treatment arms:

Core Phase Responders:

- Secukinumab 150 mg blinded
- Secukinumab 300 mg blinded

Core Phase Non-Responders:

- Secukinumab 300 mg open-label

The following study treatments were supplied:

- Secukinumab 150 mg provided in a 1 mL Pre-filled syringe (PFS) (one PFS for 150 mg dose)
- Secukinumab placebo (Placebo) provided in a 1 mL PFS

## Statistical Methods

There were two sets of primary and secondary objectives based on regional regulatory precedent and feedback. These objectives were tested in separate analysis plans.

Analysis Plan A - EU and other non- United States of America (USA) Regions

Analysis Plan B - USA

Statistical analyses of efficacy variables were performed on an intent-to-treat basis, involving all randomized patients who were assigned to study treatment (Full Analysis Set). Safety analyses were performed for all randomized patients who received at least one dose of study treatment (Safety Set).

A Sequential testing strategy was used to evaluate the study hypotheses for the primary and secondary variables while retaining a family-wise type I error of 5%.

Primary endpoint for Analysis Plan A:

The primary efficacy variable in the Analysis Plan A was the response to treatment according to ASAS40 criteria at Week 16 in TNF naïve patients. The statistical hypothesis for ASAS40 being tested was that there was no difference in the proportion of TNF naïve patients fulfilling the ASAS40 criteria at Week 16 in secukinumab with loading regimen versus placebo regimen. The primary analysis was conducted via logistic regression with treatment and stratification factor (CRP+/MRI+, CRP+/MRI-, CRP-/MRI+) as factors and baseline weight as a covariate. Odds ratios and 95% CI are comparing secukinumab regimen to placebo.

Primary endpoint for Analysis Plan B:

The primary efficacy variable in the Analysis Plan B was the response to treatment according to ASAS40 criteria at Week 52 in TNF naïve patients. The statistical hypothesis for ASAS40 being tested was that there was no difference in the proportion of TNF naïve patients fulfilling the ASAS40 criteria (and did not escape) at Week 52 in secukinumab without loading regimen versus placebo regimen. The primary analysis was conducted via logistic regression with treatment and stratification factor (CRP+/MRI+, CRP+/MRI-, CRP-/MRI+) as factors and baseline weight as a covariate. Odds ratios and 95% CI are comparing secukinumab regimen to placebo.

For the binary secondary efficacy variables, the proportion of patients meeting the ASAS40, ASAS20, ASAS 5/6, ASAS partial remission, BASDAI 50, ASDAS CRP inactive disease response was evaluated via logistic regression model with treatment and stratification factor (CRP+/MRI+, CRP+/MRI-, CRP-/MRI+) and TNF-α status as factors and baseline weight and baseline score (if appropriate) as covariates.

For the continuous secondary efficacy variables (except for SI joint edema at Week 16/52 and ASQoL at Week 52), between-treatment differences in the change from baseline in BASFI, BASDAI, ASQoL and hsCRP were evaluated using a mixed-effect model repeated measures (MMRM) model with treatment group, analysis visit, stratification factor (CRP+/MRI+, CRP+/MRI-, CRP-/MRI+) and TNF-α status as factors, baseline weight and baseline score as covariates. Treatment by analysis visit and the baseline score by analysis visit were included as interaction terms in the model. An unstructured covariance structure was assumed for the MMRM model.

The change from baseline to Week 16 in SI joint edema on MRI was evaluated using an ANCOVA model with treatment group, stratification factor (CRP+/MRI+, CRP+/MRI-, CRP-/MRI+) and TNF-α status as factors, and baseline weight and baseline inflammation score as covariates.

The change from baseline to Week 52 in ASQoL score and SI joint edema on MRI was analyzed by composite estimand strategy in which data after switch was set to extreme unfavorable value. Wilcoxon rank-sum test was used for testing the difference in distributions of the composite endpoint in secukinumab versus placebo.

## Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:
-Male or non-pregnant, non-nursing female patients at least 18 years of age
- Diagnosis of axial spondyloarthritis according to Ankylosing SpondyloArthritis International Society (ASAS) axial spondyloarthritis criteria
- objective signs of inflammation (magnetic resonance imaging (MRI) or abnormal C-reactive protein)
- active axial spondyloarthritis as assessed by total Bath Ankylosing Spondylitis Disease Activity Index >=4 cm

- Spinal pain as measured by Bath Ankylosing Spondylitis Disease Activity Index question #2 ≥ 4 cm (0-10 cm) at baseline
- Total back pain as measured by Visual Analogue scale ≥ 40 mm (0-100 mm) at baseline
- Patients should have been on at least 2 different non-steroidal anti-inflammatory drugs with an inadequate response
- Patients who have been on a Tumor Necrosis Factor (TNF) α inhibitor (not more than one) must have experienced an inadequate response

Exclusion Criteria:
- Patients with radiographic evidence for sacroiliitis, grade ≥ 2 bilaterally or grade ≥ 3 unilaterally
- Inability or unwillingness to undergo MRI
- Chest X-ray or MRI with evidence of ongoing infectious or malignant process
- Patients taking high potency opioid analgesics
- Previous exposure to secukinumab or any other biologic drug directly targeting interleukin-17 (IL-17) or IL-17 receptor
- Pregnant or nursing (lactating) women

## Participant Flow Table

### Up to Week 24

| | Secukinumab, Load, Core Phase | Secukinumab, No Load, Core Phase | Placebo, Core Phase | AIN457 150 mg Extension phase | AIN457 300 mg Extension phase | AIN457 300 mg Open Label Extension phase | Total |
|---|---|---|---|---|---|---|---|
| **Arm/Group Description** | AIN457 150 mg s.c. load, Core Phase | AIN457 150 mg s.c. no load, Core Phase | Placebo s.c., Core Phase | AIN457 150 mg Core Phase Responders who were rerandomized at week 104 to the 150 mg in the Extension phase (from Week 104 to week 208). | AIN457 150 mg Core Phase Responders who were rerandomized at week 104 to the 300 mg in the Extension phase (from Week 104 to week 208). | AIN457 150 mg Open Label Core Phase Non-Responders who were assigned at week 104 to the 300 mg Open Label in the Extension phase (from Week 104 to week 208). | |
| **Started** | 185 | 184 | 186 | 0 | 0 | 0 | 555 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Completed** | 175 | 177 | 175 | 0 | 0 | 0 | 527 |
| **Not Completed** | 10 | 7 | 11 | 0 | 0 | 0 | 28 |
| Adverse Event | 2 | 4 | 2 | 0 | 0 | 0 | 8 |
| Lack of Efficacy | 2 | 1 | 2 | 0 | 0 | 0 | 5 |
| Lost to Follow-up | 0 | 1 | 1 | 0 | 0 | 0 | 2 |
| Physician Decision | 1 | 0 | 1 | 0 | 0 | 0 | 2 |
| Protocol Violation | 1 | 0 | 0 | 0 | 0 | 0 | 1 |
| Withdrawal by Subject | 4 | 1 | 5 | 0 | 0 | 0 | 10 |

## Up to Week 52

| | **Secukinumab, Load, Core Phase** | **Secukinumab, No Load, Core Phase** | **Placebo, Core Phase** | **AIN457 150 mg Extension phase** | **AIN457 300 mg Extension phase** | **AIN457 300 mg Open Label Extension phase** | **Total** |
|---|---|---|---|---|---|---|---|
| **Arm/Group Description** | AIN457 150 mg s.c. load, Core Phase | AIN457 150 mg s.c. no load, Core Phase | Placebo s.c., Core Phase | AIN457 150 mg Core Phase Responders who were rerandomized at week 104 to the 150 mg in the Extension phase (from Week 104 to week 208). | AIN457 150 mg Core Phase Responders who were rerandomized at week 104 to the 300 mg in the Extension phase (from Week 104 to week 208). | AIN457 150 mg Open Label Core Phase Non-Responders who were assigned at week 104 to the 300 mg Open Label in the Extension phase (from | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | | | Week 104 to week 208). | |
| **Started** | 185 | 184 | 186 | 0 | 0 | 0 | 555 |
| **Completed** | 156 | 165 | 160 | 0 | 0 | 0 | 481 |
| **Not Completed** | 29 | 19 | 26 | 0 | 0 | 0 | 74 |
| Adverse Event | 4 | 5 | 3 | 0 | 0 | 0 | 12 |
| Lack of Efficacy | 10 | 7 | 11 | 0 | 0 | 0 | 28 |
| Lost to Follow-up | 1 | 1 | 1 | 0 | 0 | 0 | 3 |
| Physician Decision | 1 | 1 | 2 | 0 | 0 | 0 | 4 |
| Pregnancy | 0 | 2 | 0 | 0 | 0 | 0 | 2 |
| Protocol Violation | 1 | 0 | 0 | 0 | 0 | 0 | 1 |
| Withdrawal by Subject | 12 | 3 | 9 | 0 | 0 | 0 | 24 |

## Up to Week 104

| | **Secukinumab, Load, Core Phase** | **Secukinumab, No Load, Core Phase** | **Placebo, Core Phase** | **AIN457 150 mg Extension phase** | **AIN457 300 mg Extension phase** | **AIN457 300 mg Open Label Extension phase** | **Total** |
|---|---|---|---|---|---|---|---|
| **Arm/Group Description** | AIN457 150 mg s.c. load, Core Phase | AIN457 150 mg s.c. no load, Core Phase | Placebo s.c., Core Phase | AIN457 150 mg Core Phase Responders who were rerandomized at week 104 to the 150 mg | AIN457 150 mg Core Phase Responders who were rerandomized at week 104 to the 300 mg | AIN457 150 mg Open Label Core Phase Non-Responders who were assigned at week 104 to | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | in the Extension phase (from Week 104 to week 208). | in the Extension phase (from Week 104 to week 208). | the 300 mg Open Label in the Extension phase (from Week 104 to week 208). | |
| **Started** | 185 | 184 | 186 | 0 | 0 | 0 | 555 |
| **Completed** | 146 | 143 | 149 | 0 | 0 | 0 | 438 |
| **Not Completed** | 39 | 41 | 37 | 0 | 0 | 0 | 117 |
| Pregnancy | 0 | 2 | 1 | 0 | 0 | 0 | 3 |
| Withdrawal by Subject | 15 | 10 | 16 | 0 | 0 | 0 | 41 |
| Protocol Violation | 1 | 0 | 0 | 0 | 0 | 0 | 1 |
| Physician Decision | 1 | 2 | 3 | 0 | 0 | 0 | 6 |
| Lost to Follow-up | 2 | 3 | 1 | 0 | 0 | 0 | 6 |
| Lack of Efficacy | 13 | 12 | 11 | 0 | 0 | 0 | 36 |
| Adverse Event | 7 | 11 | 5 | 0 | 0 | 0 | 23 |
| Pt completed wk 52. Withdrawal by subject at wk 52. | 0 | 1 | 0 | 0 | 0 | 0 | 1 |

## Extension phase from wk 104 to wk 208

| | Secukinumab, Load, Core Phase | Secukinumab, No Load, Core Phase | Placebo, Core Phase | AIN457 150 mg Extension phase | AIN457 300 mg Extension phase | AIN457 300 mg Open Label Extension phase | Total |
|---|---|---|---|---|---|---|---|
| **Arm/Group Description** | AIN457 150 mg s.c. load, Core Phase | AIN457 150 mg s.c. no load, Core Phase | Placebo s.c., Core Phase | AIN457 150 mg Core Phase Responders who were rerandomized at week 104 to the 150 mg in the Extension phase (from Week 104 to week 208). | AIN457 150 mg Core Phase Responders who were rerandomized at week 104 to the 300 mg in the Extension phase (from Week 104 to week 208). | AIN457 150 mg Open Label Core Phase Non-Responders who were assigned at week 104 to the 300 mg Open Label in the Extension phase (from Week 104 to week 208). | |
| **Started** | 0 | 0 | 0 | 147 | 147 | 78 | 372 |
| **Completed** | 0 | 0 | 0 | 137 | 132 | 72 | 341 |
| **Not Completed** | 0 | 0 | 0 | 10 | 15 | 6 | 31 |
| Withdrawal by Subject | 0 | 0 | 0 | 6 | 8 | 2 | 16 |
| Physician Decision | 0 | 0 | 0 | 1 | 1 | 0 | 2 |
| Non-compliance with study treatment | 0 | 0 | 0 | 1 | 0 | 0 | 1 |
| Lost to Follow-up | 0 | 0 | 0 | 0 | 1 | 0 | 1 |
| Lack of Efficacy | 0 | 0 | 0 | 1 | 1 | 3 | 5 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Adverse Event | 0 | 0 | 0 | 1 | 4 | 1 | 6 |

## Baseline Characteristics

| | Secukinumab, Load, Core Phase | Secukinumab, No Load, Core Phase | Placebo, Core Phase | Total |
|---|---|---|---|---|
| **Arm/Group Description** | AIN457 150 mg s.c. load, Core Phase | AIN457 150 mg s.c. no load, Core Phase | Placebo s.c., Core Phase | |
| **Number of Participants [units: participants]** | 185 | 184 | 186 | 555 |
| **Age Continuous** (units: Years) Mean ± Standard Deviation | | | | |
| | 39.1±11.45 | 39.8±11.68 | 39.3±11.47 | 39.4±11.52 |
| **Sex: Female, Male** (units: Participants) Count of Participants (Not Applicable) | | | | |
| Female | 105 | 100 | 95 | 300 |
| Male | 80 | 84 | 91 | 255 |
| **Ethnicity (NIH/OMB)** (units: Participants) Count of Participants (Not Applicable) | | | | |
| Hispanic or Latino | 9 | 8 | 7 | 24 |
| Not Hispanic or Latino | 165 | 162 | 161 | 488 |
| Unknown or Not Reported | 11 | 14 | 18 | 43 |

| **Race/Ethnicity, Customized**<br>(units: Participants)<br>Count of Participants (Not Applicable) | | | | |
|---|---|---|---|---|
| American Indian or Alaska Native | 0 | 2 | 0 | 2 |
| Asian | 4 | 8 | 11 | 23 |
| Black or African American | 0 | 2 | 1 | 3 |
| White | 176 | 165 | 167 | 508 |
| Other | 5 | 7 | 7 | 19 |
| **Age Categorical**<br>(units: Participants)<br>Count of Participants (Not Applicable) | | | | |
| <=18 years | 0 | 0 | 0 | 0 |
| Between 18 and 65 years | 183 | 180 | 183 | 546 |
| >=65 years | 2 | 4 | 3 | 9 |

## Summary of Efficacy

## Primary Outcome Result(s)

### The number and percentage of TNF naive participants who achieved an Assessment of Spondylo Arthritis International Society (ASAS) 40 response at week 16

(Time Frame: Week 16)

| | **Secukinumab, Load, Core Phase** | **Secukinumab, No Load, Core Phase** | **Placebo, Core Phase** |
|---|---|---|---|
| **Arm/Group Description** | AIN457 150 mg s.c. load, Core Phase | AIN457 150 mg s.c. no | Placebo s.c., Core Phase |

| | | load, Core Phase | |
|---|---|---|---|
| **Number of Participants Analyzed [units: participants]** | 164 | 166 | 171 |
| **The number and percentage of TNF naive participants who achieved an Assessment of Spondylo Arthritis International Society (ASAS) 40 response at week 16** (units: Participants) Count of Participants (Not Applicable) | | | |
| week 16 | 68 (41.46%) | 70 (42.17%) | 50 (29.24%) |

## Statistical Analysis

| **Groups** | Secukinumab, Load, Core Phase, Placebo, Core Phase | week 16 |
|---|---|---|
| P Value | 0.0197 | unadjusted p-value |
| Method | Regression, Logistic | |
| Odds Ratio (OR) | 1.72 | |
| 95 % Confidence Interval 2-Sided | 1.09 to 2.70 | |

## Statistical Analysis

| | | |
|---|---|---|
| **Groups** | Secukinumab, No Load, Core Phase, Placebo, Core Phase | week 16 |
| P Value | 0.0146 | unadjusted p-value |
| Method | Regression, Logistic | |
| Odds Ratio (OR) | 1.76 | |
| 95 % Confidence Interval 2-Sided | 1.12 to 2.76 | |

## The number and percentage of TNF naive participants who achieved an Assessment of SpondyloArthritis International Society (ASAS) 40 response at week 52

(Time Frame: Week 52)

| | **Secukinumab, Load, Core Phase** | **Secukinumab, No Load, Core Phase** | **Placebo, Core Phase** |
|---|---|---|---|
| **Arm/Group Description** | AIN457 150 mg s.c. load, Core Phase | AIN457 150 mg s.c. no load, Core Phase | Placebo s.c., Core Phase |
| **Number of Participants Analyzed [units: participants]** | 164 | 166 | 171 |
| **The number and percentage of TNF naive participants who achieved an Assessment of SpondyloArthritis International Society (ASAS) 40 response at week 52** (units: Participants) Count of Participants (Not Applicable) | | | |

| | | | |
|---|---|---|---|
| week 52 | 58<br>(35.37%) | 66<br>(39.76%) | 34<br>(19.88%) |

## Statistical Analysis

| **Groups** | Secukinumab, Load, Core Phase,<br>Placebo, Core Phase | week 52 |
|---|---|---|
| P Value | 0.0017 | unadjusted p-value |
| Method | Regression, Logistic | |
| Odds Ratio (OR) | 2.21 | |
| 95<br>% Confidence Interval<br>2-Sided | 1.35 to 3.63 | |

## Statistical Analysis

| **Groups** | Secukinumab, No Load,<br>Core Phase,<br>Placebo, Core Phase | week 52 |
|---|---|---|
| P Value | <.0001 | unadjusted p-value |
| Method | Regression, Logistic | |
| Odds Ratio (OR) | 2.67 | |
| 95<br>% Confidence Interval<br>2-Sided | 1.64 to 4.36 | |

## Secondary Outcome Result(s)

### The number and percentage of participants who achieved an Assessment of SpondyloArthritis International Society (ASAS) 40 response

(Time Frame: Week 16 and week 52)

| | Secukinumab, Load, Core Phase | Secukinumab, No Load, Core Phase | Placebo, Core Phase |
|---|---|---|---|
| **Arm/Group Description** | AIN457 150 mg s.c. load, Core Phase | AIN457 150 mg s.c. no load, Core Phase | Placebo s.c., Core Phase |
| **Number of Participants Analyzed [units: participants]** | 185 | 184 | 186 |
| **The number and percentage of participants who achieved an Assessment of SpondyloArthritis International Society (ASAS) 40 response** (units: Participants) Count of Participants (Not Applicable) | | | |
| week 16 | 74 (40%) | 75 (40.76%) | 52 (27.96%) |
| week 52 | 62 (33.51%) | 70 (38.04%) | 36 (19.35%) |

### Statistical Analysis

| **Groups** | Secukinumab, Load, Core Phase, Placebo, Core Phase | week 16 |
|---|---|---|
| P Value | 0.0108 | unadjusted p-value |
| Method | Regression, Logistic | |
| Odds Ratio (OR) | 1.77 | |

| | | |
|---|---|---|
| 95<br>% Confidence Interval<br>2-Sided | 1.14 to 2.74 | |

## Statistical Analysis

| **Groups** | Secukinumab, No Load, Core Phase,<br>Placebo, Core Phase | week 16 |
|---|---|---|
| P Value | 0.0087 | unadjusted p-value |
| Method | Regression, Logistic | |
| Odds Ratio (OR) | 1.80 | |
| 95<br>% Confidence Interval<br>2-Sided | 1.16 to 2.78 | |

## Statistical Analysis

| **Groups** | Secukinumab, Load, Core Phase,<br>Placebo, Core Phase | |
|---|---|---|
| Non-Inferiority/Equivalence Test | Superiority | week 52 |
| P Value | 0.0016 | unadjusted p-value |
| Method | Regression, Linear | |
| Odds Ratio (OR) | 2.16 | |
| 95<br>% Confidence Interval<br>2-Sided | 1.34 to 3.49 | |

## Statistical Analysis

| | | |
|---|---|---|
| **Groups** | Secukinumab, No Load, Core Phase, Placebo, Core Phase | |
| Non-Inferiority/Equivalence Test | Superiority | week 52 |
| P Value | <.0001 | unadjusted p-value |
| Method | Regression, Linear | |
| Median Difference (Net) | 2.61 | |
| 95 % Confidence Interval 2-Sided | 1.62 to 4.19 | |

## The number and percentage of participants who achieved an Assessment of SpondyloArthritis International Society (ASAS) 20 response

(Time Frame: Week 16)

| | **Secukinumab, Load, Core Phase** | **Secukinumab, No Load, Core Phase** | **Placebo, Core Phase** |
|---|---|---|---|
| **Arm/Group Description** | AIN457 150 mg s.c. load, Core Phase | AIN457 150 mg s.c. no load, Core Phase | Placebo s.c., Core Phase |
| **Number of Participants Analyzed [units: participants]** | 185 | 184 | 186 |
| **The number and percentage of participants who achieved an Assessment of SpondyloArthritis International Society (ASAS) 20 response** (units: Participants) | | | |

| Count of Participants (Not Applicable) | | | |
|---|---|---|---|
| week 16 | 105 (56.76%) | 107 (58.15%) | 85 (45.7%) |

## Statistical Analysis

| **Groups** | Secukinumab, Load, Core Phase, Placebo, Core Phase | week 16 |
|---|---|---|
| P Value | 0.0260 | unadjusted p-value |
| Method | Regression, Logistic | |
| Odds Ratio (OR) | 1.60 | |
| 95 % Confidence Interval 2-Sided | 1.06 to 2.43 | |

## Statistical Analysis

| **Groups** | Secukinumab, No Load, Core Phase, Placebo, Core Phase | week 16 |
|---|---|---|
| P Value | 0.0149 | unadjusted p-value |
| Method | Regression, Logistic | |
| Odds Ratio (OR) | 1.68 | |
| 95 % Confidence Interval 2-Sided | 1.11 to 2.54 | |

## The number and percentage of participants who achieved an Assessment of SpondyloArthritis International Society (ASAS) 5/6 response

(Time Frame: Week 16)

| | Secukinumab, Load, Core Phase | Secukinumab, No Load, Core Phase | Placebo, Core Phase |
|---|---|---|---|
| **Arm/Group Description** | AIN457 150 mg s.c. load, Core Phase | AIN457 150 mg s.c. no load, Core Phase | Placebo s.c., Core Phase |
| **Number of Participants Analyzed [units: participants]** | 185 | 184 | 186 |
| **The number and percentage of participants who achieved an Assessment of SpondyloArthritis International Society (ASAS) 5/6 response** (units: Participants) Count of Participants (Not Applicable) | | | |
| week 16 | 74 (40%) | 66 (35.87%) | 44 (23.66%) |

## Statistical Analysis

| **Groups** | Secukinumab, Load, Core Phase, Placebo, Core Phase | week 16 |
|---|---|---|
| P Value | 0.0005 | unadjusted p-value |
| Method | Regression, Logistic | |
| Odds Ratio (OR) | 2.26 | |
| 95 % Confidence Interval 2-Sided | 1.43 to 3.58 | |

## Statistical Analysis

| | | |
|---|---|---|
| **Groups** | Secukinumab, No Load, Core Phase, Placebo, Core Phase | week 16 |
| P Value | 0.0094 | unadjusted p-value |
| Method | Regression, Logistic | |
| Odds Ratio (OR) | 1.85 | |
| 95 % Confidence Interval 2-Sided | 1.16 to 2.94 | |

## The number and percentage of participants who achieved an Assessment of SpondyloArthritis International Society Partial Remission (ASAS PR)

(Time Frame: Week 16)

| | **Secukinumab, Load, Core Phase** | **Secukinumab, No Load, Core Phase** | **Placebo, Core Phase** |
|---|---|---|---|
| **Arm/Group Description** | AIN457 150 mg s.c. load, Core Phase | AIN457 150 mg s.c. no load, Core Phase | Placebo s.c., Core Phase |
| **Number of Participants Analyzed [units: participants]** | 185 | 184 | 186 |
| **The number and percentage of participants who achieved an Assessment of SpondyloArthritis International Society Partial Remission (ASAS PR)** (units: Participants) | | | |

| Count of Participants (Not Applicable) | | | |
|---|---|---|---|
| week 16 | 40 (21.62%) | 39 (21.2%) | 13 (6.99%) |

## Statistical Analysis

| **Groups** | Secukinumab, Load, Core Phase, Placebo, Core Phase | week 16 |
|---|---|---|
| P Value | <.0001 | unadjusted p-value |
| Method | Regression, Logistic | |
| Odds Ratio (OR) | 3.80 | |
| 95 % Confidence Interval 2-Sided | 1.95 to 7.39 | |

## Statistical Analysis

| **Groups** | Secukinumab, No Load, Core Phase, Placebo, Core Phase | week 16 |
|---|---|---|
| P Value | 0.0001 | unadjusted p-value |
| Method | Regression, Logistic | |
| Odds Ratio (OR) | 3.64 | |
| 95 % Confidence Interval 2-Sided | 1.87 to 7.10 | |

## Change in Bath Ankylosing Spondylitis Functional Index (BASFI)

(Time Frame: Baseline and Week 16)

| | Secukinumab, Load, Core Phase | Secukinumab, No Load, Core Phase | Placebo, Core Phase |
|---|---|---|---|
| **Arm/Group Description** | AIN457 150 mg s.c. load, Core Phase | AIN457 150 mg s.c. no load, Core Phase | Placebo s.c., Core Phase |
| **Number of Participants Analyzed [units: participants]** | 181 | 177 | 177 |
| **Change in Bath Ankylosing Spondylitis Functional Index (BASFI)** (units: Index) Least Squares Mean ± Standard Error | | | |
| week 16 | -1.75 ± 0.202 | -1.64 ± 0.204 | -1.01 ± 0.206 |

## Statistical Analysis

| **Groups** | Secukinumab, Load, Core Phase, Placebo, Core Phase | week 16 |
|---|---|---|
| P Value | 0.0041 | unadjusted p-value |
| Method | Other MMRM | |
| Other LS Mean | -0.75 | |
| Standard Error of the mean | 0.259 | |
| 95 % Confidence Interval 2-Sided | -1.26 to -0.24 | |

## Statistical Analysis

| | | |
|---|---|---|
| **Groups** | Secukinumab, No Load, Core Phase,<br>Placebo, Core Phase | week 16 |
| P Value | 0.0143 | unadjusted p-value |
| Method | Other<br>MMRM | |
| Other<br>LS Mean | -0.64 | |
| Standard Error of the mean | 0.259 | |
| 95<br>% Confidence Interval<br>2-Sided | -1.15 to -0.13 | |

## The number and percentage of patients to achieve a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) 50 response

(Time Frame: Week 16 and 52)

| | **Secukinumab, Load, Core Phase** | **Secukinumab, No Load, Core Phase** | **Placebo, Core Phase** |
|---|---|---|---|
| **Arm/Group Description** | AIN457 150 mg s.c. load, Core Phase | AIN457 150 mg s.c. no load, Core Phase | Placebo s.c., Core Phase |
| **Number of Participants Analyzed [units: participants]** | 185 | 184 | 186 |
| **The number and percentage of patients to achieve a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) 50 response**<br>(units: Participants)<br>Count of Participants (Not Applicable) | | | |
| week 16 | 69<br>(37.3%) | 69<br>(37.5%) | 39<br>(20.97%) |
| week 52 | 57<br>(30.81%) | 65<br>(35.33%) | 37<br>(19.89%) |

## Statistical Analysis

| | | |
|---|---|---|
| **Groups** | Secukinumab, Load, Core Phase,<br>Placebo, Core Phase | week 16 |
| P Value | 0.0001 | unadjusted p-value |
| Method | Regression, Logistic | |
| Odds Ratio (OR) | 2.53 | |
| 95<br>% Confidence Interval<br>2-Sided | 1.58 to 4.07 | |

## Statistical Analysis

| | | |
|---|---|---|
| **Groups** | Secukinumab, No Load,<br>Core Phase,<br>Placebo, Core Phase | week 16 |
| P Value | 0.0002 | unadjusted p-value |
| Method | Regression, Logistic | |
| Odds Ratio (OR) | 2.43 | |
| 95<br>% Confidence Interval<br>2-Sided | 1.51 to 3.89 | |

## Statistical Analysis

| | | |
|---|---|---|
| **Groups** | Secukinumab, Load, Core Phase,<br>Placebo, Core Phase | week 52 |
| P Value | 0.0056 | unadjusted p-value |

| | |
|---|---|
| Method | Regression, Logistic |
| Odds Ratio (OR) | 1.99 |
| 95 % Confidence Interval 2-Sided | 1.22 to 3.24 |

## Statistical Analysis

| | | |
|---|---|---|
| **Groups** | Secukinumab, No Load, Core Phase, Placebo, Core Phase | week 52 |
| P Value | 0.0005 | unadjusted p-value |
| Method | Regression, Logistic | |
| Odds Ratio (OR) | 2.34 | |
| 95 % Confidence Interval 2-Sided | 1.45 to 3.78 | |

## Change in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

(Time Frame: Baseline and Week 16)

| | **Secukinumab, Load, Core Phase** | **Secukinumab, No Load, Core Phase** | **Placebo, Core Phase** |
|---|---|---|---|
| **Arm/Group Description** | AIN457 150 mg s.c. load, Core Phase | AIN457 150 mg s.c. no load, Core Phase | Placebo s.c., Core Phase |
| **Number of Participants Analyzed [units: participants]** | 181 | 177 | 177 |
| **Change in Bath Ankylosing Spondylitis** | | | |

| **Disease Activity Index (BASDAI)**<br>(units: scores on a scale)<br>Least Squares Mean ± Standard Error | | | |
|---|---|---|---|
| week 16 | -2.35 ± 0.201 | -2.43 ± 0.203 | -1.46 ± 0.205 |

## Statistical Analysis

| **Groups** | Secukinumab, Load, Core Phase,<br>Placebo, Core Phase | week 16 |
|---|---|---|
| P Value | 0.0006 | unadjusted p-value |
| Method | Other<br>mixed model repeated measures (MMRM) | |
| Other<br>LS Mean of treatment difference | -0.89 | |
| Standard Error of the mean | 0.256 | |
| 95<br>% Confidence Interval<br>2-Sided | -1.39 to -0.38 | |

## Statistical Analysis

| **Groups** | Secukinumab, No Load,<br>Core Phase,<br>Placebo, Core Phase | week 16 |
|---|---|---|
| P Value | 0.0002 | unadjusted p-value |
| Method | Other<br>mixed model repeated measures (MMRM) | |

| | |
|---|---|
| Other<br>LS Mean of Treatment Difference | -0.97 |
| Standard Error of the mean | 0.255 |
| 95<br>% Confidence Interval<br>2-Sided | -1.47 to -0.47 |

## Change in Ankylosing Spondylitis Quality of Life (ASQoL) scores at week 16

(Time Frame: Baseline and Week 16)

| | Secukinumab, Load, Core Phase | Secukinumab, No Load, Core Phase | Placebo, Core Phase |
|---|---|---|---|
| **Arm/Group Description** | AIN457 150 mg s.c. load, Core Phase | AIN457 150 mg s.c. no load, Core Phase | Placebo s.c., Core Phase |
| **Number of Participants Analyzed [units: participants]** | 181 | 176 | 177 |
| **Change in Ankylosing Spondylitis Quality of Life (ASQoL) scores at week 16**<br>(units: Scores on a scale)<br>Least Squares Mean ± Standard Error | | | |
| week 16 | -3.45 ± 0.408 | -3.62 ± 0.414 | -1.84 ± 0.421 |

## Statistical Analysis

| | | |
|---|---|---|
| **Groups** | Secukinumab, Load, Core Phase,<br>Placebo, Core Phase | week 16 |
| P Value | 0.0008 | unadjusted p-value |

| | |
|---|---|
| Method | Other<br>MMRM |
| Other<br>LS Mean | -1.61 |
| Standard Error of the mean | 0.478 |
| 95<br>% Confidence Interval<br>2-Sided | -2.54 to -0.67 |

## Statistical Analysis

| | | |
|---|---|---|
| **Groups** | Secukinumab, No Load, Core Phase,<br>Placebo, Core Phase | week 16 |
| P Value | 0.0002 | unadjusted p-value |
| Method | Other<br>MMRM | |
| Other<br>LS Mean | -1.78 | |
| Standard Error of the mean | 0.479 | |
| 95<br>% Confidence Interval<br>2-Sided | -2.72 to -0.84 | |

## Change in Ankylosing Spondylitis Quality of Life (ASQoL) scores at week 52

(Time Frame: Baseline and Week 52)

| | Secukinumab, Load, Core Phase | Secukinumab, No Load, Core Phase | Placebo, Core Phase |
|---|---|---|---|
| **Arm/Group Description** | AIN457 150 mg s.c. load, Core Phase | AIN457 150 mg s.c. no load, Core Phase | Placebo s.c., Core Phase |

| | | | |
|---|---|---|---|
| **Number of Participants Analyzed [units: participants]** | 83 | 88 | 54 |
| **Change in Ankylosing Spondylitis Quality of Life (ASQoL) scores at week 52** (units: Scores on a scale) Mean ± Standard Deviation | | | |
| week 52 | -7.1 ± 4.77 | -7.6 ± 5.38 | -6.4 ± 4.64 |

## Statistical Analysis

| | | |
|---|---|---|
| **Groups** | Secukinumab, Load, Core Phase, Placebo, Core Phase | |
| P Value | 0.0012 | unadjusted p-value |
| Method | Wilcoxon (Mann-Whitney) Wilcoxon rank sum test | The endpoint was analyzed by composite estimand strategy. Extreme unfavorable value is assigned for patients with treatment escape or missing data. |

## Statistical Analysis

| | | |
|---|---|---|
| **Groups** | Secukinumab, No Load, Core Phase, Placebo, Core Phase | |
| P Value | <.0001 | unadjusted p-value |
| Method | Wilcoxon (Mann-Whitney) | The endpoint was analyzed by composite estimand strategy. Extreme unfavorable value is assigned for patients |

with treatment escape or missing data.

## The number and percentage of patients who achieved an Ankylosing Spondylitis Disease Activity Score (ASDAS)-C-Reactive Protein (CRP) inactive disease

(Time Frame: Week 52)

| | Secukinumab, Load, Core Phase | Secukinumab, No Load, Core Phase | Placebo, Core Phase |
|---|---|---|---|
| **Arm/Group Description** | AIN457 150 mg s.c. load, Core Phase | AIN457 150 mg s.c. no load, Core Phase | Placebo s.c., Core Phase |
| **Number of Participants Analyzed [units: participants]** | 185 | 184 | 186 |
| **The number and percentage of patients who achieved an Ankylosing Spondylitis Disease Activity Score (ASDAS)-C-Reactive Protein (CRP) inactive disease** (units: Participants) Count of Participants (Not Applicable) | | | |
| week 52 | 29 (15.68%) | 44 (23.91%) | 19 (10.22%) |

## Statistical Analysis

| **Groups** | Secukinumab, Load, Core Phase, Placebo, Core Phase | week 52 |
|---|---|---|
| P Value | 0.0577 | unadjusted p-value |

| | |
|---|---|
| Method | Regression, Logistic |
| Odds Ratio (OR) | 1.84 |
| 95 % Confidence Interval 2-Sided | 0.98 to 3.45 |

## Statistical Analysis

| | | |
|---|---|---|
| **Groups** | Secukinumab, No Load, Core Phase, Placebo, Core Phase | week 52 |
| P Value | 0.0003 | unadjusted p-value |
| Method | Regression, Logistic | |
| Odds Ratio (OR) | 2.99 | |
| 95 % Confidence Interval 2-Sided | 1.65 to 5.41 | |

## Change in high sensitivity C-reactive protein

(Time Frame: Baseline and Week 16)

| | **Secukinumab, Load, Core Phase** | **Secukinumab, No Load, Core Phase** | **Placebo, Core Phase** |
|---|---|---|---|
| **Arm/Group Description** | AIN457 150 mg s.c. load, Core Phase | AIN457 150 mg s.c. no load, Core Phase | Placebo s.c., Core Phase |
| **Number of Participants Analyzed [units: participants]** | 180 | 176 | 175 |
| **Change in high sensitivity C-reactive** | | | |

| **protein**<br>(units: ratio)<br>Least Squares Mean ± Standard Error | | | |
|---|---|---|---|
| week 16 | 0.64 ± 1.078 | 0.64 ± 1.079 | 0.91 ± 1.080 |

## Statistical Analysis

| **Groups** | Secukinumab, Load, Core Phase,<br>Placebo, Core Phase | week 16 |
|---|---|---|
| P Value | 0.0002 | unadjusted p-value |
| Method | Other<br>MMRM | |
| Other<br>Relative Treatment Effect | 0.70 | |
| 95<br>% Confidence Interval<br>2-Sided | 0.58 to 0.84 | |

## Statistical Analysis

| **Groups** | Secukinumab, No Load,<br>Core Phase,<br>Placebo, Core Phase | week 16 |
|---|---|---|
| P Value | 0.0002 | unadjusted p-value |
| Method | Other<br>MMRM | |
| Other<br>Relative Treatment Effect | 0.70 | |
| 95<br>% Confidence Interval | 0.58 to 0.84 | |

## Change in Short Form-36 Physical Component Summary (SF-36 PCS)

(Time Frame: Baseline and Week 16)

| | Secukinumab, Load, Core Phase | Secukinumab, No Load, Core Phase | Placebo, Core Phase |
|---|---|---|---|
| **Arm/Group Description** | AIN457 150 mg s.c. load, Core Phase | AIN457 150 mg s.c. no load, Core Phase | Placebo s.c., Core Phase |
| **Number of Participants Analyzed [units: participants]** | 182 | 176 | 178 |
| **Change in Short Form-36 Physical Component Summary (SF-36 PCS)** (units: Scores on a Scale) Least Squares Mean ± Standard Error | | | |
| week 16 | 5.71 ± 0.683 | 5.57 ± 0.694 | 2.93 ± 0.705 |

## Statistical Analysis

| **Groups** | Secukinumab, Load, Core Phase, Placebo, Core Phase | week 16 |
|---|---|---|
| P Value | 0.0006 | unadjusted p-value |
| Method | ANCOVA | |
| Other LS Mean of Treatment Difference | 2.77 | |
| Standard Error of the mean | 0.799 | |
| 95 % Confidence Interval 2-Sided | 1.20 to 4.34 | |

## Statistical Analysis

| | | |
|---|---|---|
| **Groups** | Secukinumab, No Load, Core Phase,<br>Placebo, Core Phase | week 16 |
| P Value | 0.0011 | unadjusted p-value |
| Method | ANCOVA<br>LS Mean of Treatment Difference | |
| Other<br>LS Mean of Treatment Difference | 2.64 | |
| Standard Error of the mean | 0.803 | |
| 95<br>% Confidence Interval<br>2-Sided | 1.06 to 4.22 | |

## Change in Sacroiliac Joint Edema - week 16

(Time Frame: Baseline and Week 16)

| | **Secukinumab, Load, Core Phase** | **Secukinumab, No Load, Core Phase** | **Placebo, Core Phase** |
|---|---|---|---|
| **Arm/Group Description** | AIN457 150 mg s.c. load, Core Phase | AIN457 150 mg s.c. no load, Core Phase | Placebo s.c., Core Phase |
| **Number of Participants Analyzed [units: participants]** | 180 | 177 | 174 |
| **Change in Sacroiliac Joint Edema - week 16**<br>(units: Scores on a Scale)<br>Mean ± Standard Error | | | |
| | -1.68 ± 0.24 | -1.03 ± 0.18 | -0.39 ± 0.15 |

## Statistical Analysis

| | | |
|---|---|---|
| **Groups** | Secukinumab, Load, Core Phase,<br>Placebo, Core Phase | week 16 |
| P Value | <0.0001 | unadjusted p-value |
| Method | ANCOVA | |

## Statistical Analysis

| | | |
|---|---|---|
| **Groups** | Secukinumab, No Load, Core Phase,<br>Placebo, Core Phase | week 16 |
| P Value | <0.0001 | unadjusted p-value |
| Method | ANCOVA | |

## Change in Sacroiliac Joint Edema - week 52

(Time Frame: Baseline and Week 52)

| | **Secukinumab, Load, Core Phase** | **Secukinumab, No Load, Core Phase** | **Placebo, Core Phase** |
|---|---|---|---|
| **Arm/Group Description** | AIN457 150 mg s.c. load, Core Phase | AIN457 150 mg s.c. no load, Core Phase | Placebo s.c., Core Phase |
| **Number of Participants Analyzed [units: participants]** | 81 | 87 | 53 |
| **Change in Sacroiliac Joint Edema - week 52** (units: Scores on a scale) Mean ± Standard Deviation | | | |
| week 52 | -2.9 ± 4.54 | -1.9 ± 3.40 | -0.1 ± 1.97 |

## Statistical Analysis

| Groups | Secukinumab, Load, Core Phase,<br>Placebo, Core Phase | |
|---|---|---|
| P Value | <.0001 | unadjusted p-value |
| Method | Wilcoxon (Mann-Whitney) | The endpoint was analyzed by composite estimand strategy. Extreme unfavorable value is assigned for patients with treatment escape or missing data. |

### Statistical Analysis

| Groups | Secukinumab, No Load, Core Phase,<br>Placebo, Core Phase | |
|---|---|---|
| P Value | <.0001 | unadjusted p-value |
| Method | Wilcoxon (Mann-Whitney) | The endpoint was analyzed by composite estimand strategy. Extreme unfavorable value is assigned for patients with treatment escape or missing data. |

## Safety Results

### All-Cause Mortality

| | Any AIN457 150 mg, in Core Phase and Extension | Any AIN457 300 mg in Extension Phase N = 254 | Any AIN457, In Core Phase and Extension | Placebo, Core Phase N = 186 |
|---|---|---|---|---|

| | Phase N = 543 | | Phase N = 543 | |
|---|---|---|---|---|
| **Arm/Group Description** | Includes patients originally randomized to AIN457 150 mg (Load and No Load) at baseline and placebo patients switched to AIN457 150 mg before or at W52 (AEs occurring after the switch) who either were re-randomized (Core Phase Responders) to AIN457 150 mg at W104 or did not participate in the Extension Phase. | Includes patients re-randomized (Core Phase Responders) or re-assigned (Core Phase Non-Responders) to AIN457 300 mg at W104 (Extension Phase) and patients re-randomized (Core Phase Responders) to AIN457 150 mg at W104 who up-titrated to AIN457 300 mg (only AEs occurring after up-titration). | Includes patients randomized or switched (AEs occurring after the switch) to AIN457 150 mg (Load and No Load) who either were re-randomized (Core Phase Responders) to AIN457 150 mg or AIN457 300 mg at W104 or did not participate in the Extension Phase. | Includes patients originally randomized to Placebo (AEs until the time of a switch to AIN457 150 mg) |
| **Total participants affected** | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) |

## Serious Adverse Events by System Organ Class

| | |
|---|---|
| **Time Frame** | Adverse events are reported from first dose of study treatment until end of study treatment plus 12 wks post-treatment, up to a maximum timeframe of 1520 days (approx. 4.2 years). Safety results summarize long term data for all patients for the entire period of their study participation, which, for the majority of pts, combines the core phase and the extension phase (not all pts participated in the extension). The table is presented by dose group, AIN457 150 mg and AIN457 300 mg and placebo. |

| | |
|---|---|
| **Additional Description** | Any exposure to AIN457 in the core phase is presented as Any AIN457 150 mg, regardless if patients were initially assigned to Load or No Load. Considering the total length of exposure to AIN457 150 mg, the effect of initial loading regimen during the first 4 weeks of treatment is considered negligible. Pts. may have switched from placebo to 150 mg or from 150 mg to 300 mg during the course of the study. Therefore, some pts are counted in more than 1 dose group, depending on the AE timing. |
| **Source Vocabulary for Table Default** | MedDRA (23.1) |
| **Assessment Type for Table Default** | Systematic Assessment |

| | **Any AIN457 150 mg, in Core Phase and Extension Phase N = 543** | **Any AIN457 300 mg in Extension Phase N = 254** | **Any AIN457, In Core Phase and Extension Phase N = 543** | **Placebo, Core Phase N = 186** |
|---|---|---|---|---|
| **Arm/Group Description** | Includes patients originally randomized to AIN457 150 mg (Load and No Load) at baseline and placebo patients switched to AIN457 150 mg before or at W52 (AEs occurring after the switch) who either were re-randomized (Core Phase Responders) to AIN457 150 mg at W104 | Includes patients re-randomized (Core Phase Responders) or re-assigned (Core Phase Non-Responders) to AIN457 300 mg at W104 (Extension Phase) and patients re-randomized (Core Phase Responders) to AIN457 150 mg at W104 who up-titrated to AIN457 300 mg (only AEs | Includes patients randomized or switched (AEs occurring after the switch) to AIN457 150 mg (Load and No Load) who either were re-randomized (Core Phase Responders) to AIN457 150 mg or AIN457 300 mg at W104 or did not participate in the Extension Phase. | Includes patients originally randomized to Placebo (AEs until the time of a switch to AIN457 150 mg) |

| | | | | |
|---|---|---|---|---|
| | or did not participate in the Extension Phase. | occurring after up-titration). | | |
| **Total participants affected** | 48 (8.84%) | 11 (4.33%) | 58 (10.68%) | 8 (4.30%) |
| **Blood and lymphatic system disorders** | | | | |
| Anaemia | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| **Cardiac disorders** | | | | |
| Acute coronary syndrome | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (0.54%) |
| Aortic valve incompetence | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Myocardial infarction | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (0.54%) |
| **Eye disorders** | | | | |
| Iridocyclitis | 1 (0.18%) | 1 (0.39%) | 2 (0.37%) | 0 (0.00%) |
| **Gastrointestinal disorders** | | | | |
| Abdominal pain | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Anal fistula | 0 (0.00%) | 1 (0.39%) | 1 (0.18%) | 0 (0.00%) |
| Appendiceal mucocoele | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Colitis | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Colitis ulcerative | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Crohn's disease | 2 (0.37%) | 1 (0.39%) | 3 (0.55%) | 0 (0.00%) |
| Diarrhoea | 0 (0.00%) | 1 (0.39%) | 1 (0.18%) | 0 (0.00%) |
| Inguinal hernia | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Lower gastrointestinal haemorrhage | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |

| | | | | |
|---|---|---|---|---|
| **General disorders and administration site conditions** | | | | |
| Pyrexia | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (0.54%) |
| **Hepatobiliary disorders** | | | | |
| Biliary colic | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Cholelithiasis | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Drug-induced liver injury | 0 (0.00%) | 1 (0.39%) | 1 (0.18%) | 0 (0.00%) |
| Hepatitis acute | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| **Infections and infestations** | | | | |
| Anal abscess | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Appendicitis | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Atypical pneumonia | 0 (0.00%) | 1 (0.39%) | 1 (0.18%) | 0 (0.00%) |
| Device related infection | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Diverticulitis | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Eczema infected | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Epiglottitis | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Gastroenteritis | 1 (0.18%) | 1 (0.39%) | 2 (0.37%) | 0 (0.00%) |
| Peritonsillar abscess | 0 (0.00%) | 1 (0.39%) | 1 (0.18%) | 0 (0.00%) |
| Pharyngitis streptococcal | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Pneumonia | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Postoperative wound infection | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Sepsis | 0 (0.00%) | 1 (0.39%) | 1 (0.18%) | 0 (0.00%) |
| Subcutaneous abscess | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |

| | | | | |
|---|---|---|---|---|
| Tonsillitis | 3 (0.55%) | 0 (0.00%) | 3 (0.55%) | 0 (0.00%) |
| Urinary tract infection | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Vaccination site cellulitis | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Viral tracheitis | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (0.54%) |
| **Injury, poisoning and procedural complications** | | | | |
| Brain contusion | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Clavicle fracture | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (0.54%) |
| Hip fracture | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Meniscus injury | 1 (0.18%) | 1 (0.39%) | 2 (0.37%) | 0 (0.00%) |
| Skin laceration | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Tendon injury | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Wound dehiscence | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Wrist fracture | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| **Investigations** | | | | |
| Arthroscopy | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| **Metabolism and nutrition disorders** | | | | |
| Diabetes mellitus | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Diabetic ketoacidosis | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Electrolyte imbalance | 0 (0.00%) | 1 (0.39%) | 1 (0.18%) | 0 (0.00%) |
| Hypoalbuminaemia | 0 (0.00%) | 1 (0.39%) | 1 (0.18%) | 0 (0.00%) |
| **Musculoskeletal and connective tissue disorders** | | | | |
| Arthralgia | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (0.54%) |

| | | | | |
|---|---|---|---|---|
| Arthritis | 3 (0.55%) | 0 (0.00%) | 3 (0.55%) | 0 (0.00%) |
| Back disorder | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Back pain | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 1 (0.54%) |
| Intervertebral disc disorder | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Osteoarthritis | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Synovitis | 1 (0.18%) | 1 (0.39%) | 2 (0.37%) | 0 (0.00%) |
| **Neoplasms benign, malignant and unspecified (incl cysts and polyps)** | | | | |
| Acrochordon | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Basal cell carcinoma | 0 (0.00%) | 1 (0.39%) | 1 (0.18%) | 0 (0.00%) |
| Fibroadenoma of breast | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Malignant melanoma | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Rectal adenocarcinoma | 0 (0.00%) | 1 (0.39%) | 1 (0.18%) | 0 (0.00%) |
| **Nervous system disorders** | | | | |
| Myelopathy | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Sciatica | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Spinal claudication | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Syncope | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| **Psychiatric disorders** | | | | |
| Substance-induced mood disorder | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Suicide attempt | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| **Renal and urinary disorders** | | | | |

| | | | | |
|---|---|---|---|---|
| Calculus urinary | 0 (0.00%) | 1 (0.39%) | 1 (0.18%) | 0 (0.00%) |
| IgA nephropathy | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Nephrolithiasis | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| **Reproductive system and breast disorders** | | | | |
| Bartholin's cyst | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (0.54%) |
| Cervix enlargement | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (0.54%) |
| Endometrial disorder | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (0.54%) |
| Ovarian cyst | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Vaginal prolapse | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (0.54%) |
| Varicocele | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| **Respiratory, thoracic and mediastinal disorders** | | | | |
| Nasal septum deviation | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Pneumomediastinum | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Pneumothorax | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| **Skin and subcutaneous tissue disorders** | | | | |
| Skin disorder | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| **Vascular disorders** | | | | |
| Aortic aneurysm | 1 (0.18%) | 0 (0.00%) | 1 (0.18%) | 0 (0.00%) |
| Arteriosclerosis | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (0.54%) |

## Other Adverse Events by System Organ Class

| | |
|---|---|
| **Time Frame** | Adverse events are reported from first dose of study treatment until end of study treatment plus 12 wks post-treatment, up to a maximum timeframe of 1520 days (approx. 4.2 years). Safety results summarize long term data for all patients for the entire period of their study participation, which, for the majority of pts, combines the core phase and the extension phase (not all pts participated in the extension). The table is presented by dose group, AIN457 150 mg and AIN457 300 mg and placebo. |
| **Additional Description** | Any exposure to AIN457 in the core phase is presented as Any AIN457 150 mg, regardless if patients were initially assigned to Load or No Load. Considering the total length of exposure to AIN457 150 mg, the effect of initial loading regimen during the first 4 weeks of treatment is considered negligible. Pts. may have switched from placebo to 150 mg or from 150 mg to 300 mg during the course of the study. Therefore, some pts are counted in more than 1 dose group, depending on the AE timing. |
| **Source Vocabulary for Table Default** | MedDRA (23.1) |
| **Assessment Type for Table Default** | Systematic Assessment |
| **Frequent Event Reporting Threshold** | 5% |

| | **Any AIN457 150 mg, in Core Phase and Extension Phase N = 543** | **Any AIN457 300 mg in Extension Phase N = 254** | **Any AIN457, In Core Phase and Extension Phase N = 543** | **Placebo, Core Phase N = 186** |
|---|---|---|---|---|
| **Arm/Group Description** | Includes patients originally randomized to AIN457 150 mg (Load and No Load) at baseline and placebo patients switched to AIN457 150 mg before or at W52 (AEs occurring after the switch) | Includes patients re-randomized (Core Phase Responders) or re-assigned (Core Phase Non-Responders) to AIN457 300 mg at W104 (Extension Phase) and patients re-randomized (Core Phase | Includes patients randomized or switched (AEs occurring after the switch) to AIN457 150 mg (Load and No Load) who either were re-randomized (Core Phase Responders) to AIN457 150 mg or AIN457 300 mg at | Includes patients originally randomized to Placebo (AEs until the time of a switch to AIN457 150 mg) |

| | who either were re-randomized (Core Phase Responders) to AIN457 150 mg at W104 or did not participate in the Extension Phase. | Responders) to AIN457 150 mg at W104 who up-titrated to AIN457 300 mg (only AEs occurring after up-titration). | W104 or did not participate in the Extension Phase. | |
|---|---|---|---|---|
| **Total participants affected** | 320 (58.93%) | 74 (29.13%) | 335 (61.69%) | 67 (36.02%) |
| **Gastrointestinal disorders** | | | | |
| Diarrhoea | 55 (10.13%) | 6 (2.36%) | 61 (11.23%) | 10 (5.38%) |
| **Infections and infestations** | | | | |
| Bronchitis | 23 (4.24%) | 6 (2.36%) | 28 (5.16%) | 2 (1.08%) |
| Nasopharyngitis | 137 (25.23%) | 33 (12.99%) | 146 (26.89%) | 32 (17.20%) |
| Pharyngitis | 27 (4.97%) | 5 (1.97%) | 31 (5.71%) | 1 (0.54%) |
| Sinusitis | 30 (5.52%) | 5 (1.97%) | 34 (6.26%) | 3 (1.61%) |
| Upper respiratory tract infection | 65 (11.97%) | 16 (6.30%) | 77 (14.18%) | 13 (6.99%) |
| Urinary tract infection | 38 (7.00%) | 9 (3.54%) | 42 (7.73%) | 4 (2.15%) |
| **Musculoskeletal and connective tissue disorders** | | | | |
| Arthralgia | 43 (7.92%) | 6 (2.36%) | 48 (8.84%) | 9 (4.84%) |
| Back pain | 36 (6.63%) | 3 (1.18%) | 38 (7.00%) | 3 (1.61%) |
| **Nervous system disorders** | | | | |
| Headache | 61 (11.23%) | 7 (2.76%) | 65 (11.97%) | 9 (4.84%) |

| | | | | |
|---|---|---|---|---|
| **Vascular disorders** | | | | |
| Hypertension | 29 (5.34%) | 5 (1.97%) | 34 (6.26%) | 3 (1.61%) |

## Conclusion:

Secukinumab 150 mg Load and No Load demonstrated a rapid onset of response and superior efficacy over placebo in the treatment of patients with Non-radiographic axial spondyloarthritis (nr-axSpA) across measures of clinical response, Quality of Life (QoL) and markers of inflammation. For many of the efficacy endpoints, an earlier onset of response was observed with secukinumab 150 mg Load compared to secukinumab 150 mg No Load. For both secukinumab 150 mg Load and No Load, a trend towards better efficacy of secukinumab vs. placebo across efficacy endpoints were reported through Week 52, regardless of previous Tumor Necrosis Factor inhibitor (TNFi) use. Secukinumab 150 mg Load and No Load demonstrated efficacy through 52 weeks of treatment in all subgroups of patients with objective signs of inflammation based on abnormal C-reactive protein (CRP) or Magnetic resonance imaging (MRI) or both abnormal CRP and MRI at baseline. The safety profile of secukinumab 150 mg (with or without loading) showed no new or unexpected safety signals and was consistent with the overall safety profile of secukinumab, based on the extensive safety data across multiple indications including psoriasis, psoriatic arthritis, and ankylosing spondylitis.

The safety profile of secukinumab 150 mg showed no new or unexpected safety signals during the entire treatment period (including the extension phase), and was consistent with the overall safety profile of secukinumab. The safety profile of secukinumab 300 mg showed no new or unexpected safety signals and was consistent with the overall safety profile of secukinumab.

## Date of Clinical Trial Report

Final 1-Sep-2021