Sponsor

Novartis

Generic Drug Name

Secukinumab

Trial Indications

Active axial spondyloarthritis (axSpA)

Protocol Number

CAIN457HDE01

Protocol Title

A randomized, open label multicenter trial to investigate the efficacy of a treat-to-target (T2T) treatment strategy with secukinumab (AIN457) as a first-line biologic compared to a standard-of-care (SOC) treatment over 36 weeks in patients with active axial spondyloarthritis (axSpA)

Clinical Trial Phase

Phase 3

Phase of Drug Development

Phase IV

Study Start/End Dates

Study Start Date: June 04, 2019 (Actual)
Primary Completion Date: February 04, 2022 (Actual)
Study Completion Date: September 22, 2022 (Actual)

Reason for Termination (If applicable)

Not applicable

Study Design/Methodology

This was a randomized, parallel-group, open-label, multicenter study in patients with active axSpA. The aim of the study was to demonstrate that the efficacy of a T2T approach (with secukinumab as a first-line biologic) was superior to a SOC approach in terms of achieving strong clinical efficacy in patients with active axSpA who were naïve to biological therapy and who had an inadequate response to prior non-steroidal anti-inflammatory drug (NSAID) treatment.

Centers

47 centers in 2 countries: Germany(34), France(13)

Objectives:

Primary objective:

- 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 Assessment of SpondyloArthritis International Society criteria 40 (ASAS40) response at Week 24.

Secondary objectives:

- 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 12.
- To demonstrate that the efficacy of the T2T (with secukinumab as first-line biologic) is superior to the SOC approach based on the percentage of patients achieving an Ankylosing Spondylitis Disease Activity Score (ASDAS) clinically important improvement (defined as change from Baseline (BSL) of ≥ 1.1) at Week 12 and Week 24.

- To demonstrate that the efficacy of the T2T (with secukinumab as first-line biologic) is superior to the SOC approach based on the percentage of patients achieving an ASDAS major improvement (defined as change from BSL of ≥ 2.0) at Week 12 and Week 24.
- 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 ASDAS < 1.3 at Week 12 and Week 24.
- 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 ASDAS < 2.1 (low disease activity) at Week 12 and Week 24.
- 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 ASAS20, ASAS partial remission (PR), and Bath Ankylosing Spondylitis Disease Activity Index response 50% (BASDAI 50) responses at Week 12 and Week 24.
- To demonstrate that the T2T approach (with secukinumab as first-line biologic) is superior to the SOC approach in terms of improvement of disease activity, function, axial mobility, and quality of life measures at Week 12 and Week 24 as compared to Baseline according to:
    - BASDAI
    - ASDAS
    - C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)
    - Bath Ankylosing Spondylitis Functional Index (BASFI)
    - Bath Ankylosing Spondylitis Metrology Index (BASMI) and chest expansion
    - Global assessment of disease activity (patient/physician) and general pain on a visual analog scale (VAS)
    - Ankylosing Spondyloarthritis International Society Health Index (ASAS-HI)
    - Short Form Health Survey (SF)-36
    - Ankylosing Spondylitis Quality of Life (ASQoL)
    - Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-Fatigue)
- To demonstrate overall safety and tolerability of secukinumab.

Test Product, Doses, and Mode of Administration

Secukinumab, 150 – 300 mg, subcutaneous (s.c.) injection

Statistical Methods

All categorical data were presented in terms of frequencies and percentages. Summaries of continuous data were presented in terms of mean, standard deviation (SD), median, lower and upper quartiles (for most variables), minimum and maximum, the number of missing data points (for most variables) and the number of non-missing data points.

For descriptive statistics, the following number of decimal places were used: arithmetic mean, median, lower quartile and upper quartile to one more decimal places than the raw data; minimum and maximum to the same number of decimal places as the raw data and SD to two more decimal places than the raw data. Percentages were presented to one decimal place.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:
• Diagnosis of Axial Spondyloarthritis, axSpA (either Non-Radiographic Axial Spondyloarthritis or Radiographic Axial Spondyloarthritis) fulfilling the Ankylosing Spondyloarthritis International Society classification criteria for axSpA
• Active disease as defined by having an Ankylosing Spondylitis Disease Activity Score ≥ 2.1 at Screening and Baseline despite concurrent Non-Steroidal Anti-Inflammatory Drug (NSAID) therapy, or intolerance/contraindication to NSAIDs.
• Objective signs of inflammation at Screening as defined by: Magnetic Resonance Imaging (MRI) of sacroiliac joints performed up to 3 months prior to screening showing acute inflammatory lesion(s), OR elevated quick C-reactive Protein (CRP) (> 5 mg/L), OR MRI showing acute inflammatory lesion(s) in the sacroiliac joints and spine performed during screening period.
• Inadequate response to NSAIDs

Exclusion Criteria:
• Previous exposure to secukinumab or other biologic drug directly targeting Interleukin(IL)-17 or IL-17 receptor.
• Patients who have previously been treated with Tumor Necrosis Factor Alpha inhibitors (investigational or approved).
• Patients treated with any cell-depleting therapies.
• Active ongoing inflammatory diseases or underlying metabolic, hematologic, renal, hepatic, pulmonary, neurologic, endocrine, cardiac, infectious or gastrointestinal conditions, which in the opinion of the investigator immunosuppressed the patient and/or places the patient at unacceptable risk for participation in an immunomodulatory therapy.
• History of clinically significant liver disease or liver injury
• History of renal trauma, glomerulonephritis, or patients with one kidney only, or a serum creatinine level exceeding 1.8 mg/dL (159.12 µmol/L).
• Active systemic infections during the last 2 weeks (exception: common cold) prior to randomization.
• History of ongoing, chronic or recurrent infectious disease or evidence of tuberculosis (TB) infection

• Patients positive for human immunodeficiency virus, hepatitis B or hepatitis C

• Life vaccinations within 6 weeks prior to Baseline or planned vaccination during study participation until 12 weeks after last study treatment administration.
Other protocol-defined inclusion/exclusion criteria may apply.

Participant Flow Table

Overall Study

	Treat-to-Target (T2T)	Standard-of-care (SOC)	Total
Arm/Group Description	Treat To Target approach with secukinumab as first line biologic	Patients received treatment according to local practice standards by their treating physician following the current treatment recommendations	
Started	155	149	304
Completed	143	138	281
Not Completed	12	11	23
Adverse Event	1	0	1
Lost to Follow-up	7	4	11
Physician Decision	1	0	1
Withdrawal by Subject	3	7	10

Baseline Characteristics

	Treat-to-Target (T2T)	Standard-of-care (SOC)	Total
Arm/Group Description	Participants received secukinumab at a dose of 150 milligrams (mg) as	Patients received treatment according to local practice standards by their treating	

	subcutaneous (s.c.) injection at 150 mg dose at Baseline, Week 1, 2, 3, 4 and 8. From Week 12, only responders continued to receive 4-weekly doses until Week 32 if they maintained the response. In the event these patients experienced a loss of response from Week 24, they were escalated to secukinumab 300 mg s.c. every 4 weeks until Week 32. Patients who were non-responders at Week 12 received 4-weekly secukinumab 300 mg s.c. until Week 24. From Week 24, only responders continued to receive 4-weekly secukinumab 300 mg s.c. until Week 32. Patients who were non-responders to secukinumab 300 mg at Week 24 received biweekly adalimumab biosimilar 40 mg s.c. until Week 34.	physician following the current treatment recommendations	
Number of Participants [units: participants]	155	149	304
Baseline Analysis Population Description	Full analysis set (FAS) comprised all patients to whom study treatment/reference treatment has been assigned by randomization. According to the intent to treat principle, patients were analyzed according to the treatment they have been assigned to during the randomization procedure.		
Age Continuous (units: Years)			

Analysis Population Type: Participants Mean ± Standard Deviation			
	40.0±12.03	38.6±12.17	39.3±12.10
Age Categorical (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)			
<=18 years	0	0	0
Between 18 and 65 years	149	144	293
>=65 years	6	5	11
Sex: Female, Male (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)			
Female	59	51	110
Male	96	98	194
Race/Ethnicity, Customized (units: Participants) Analysis Population Type: Participants			
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

Primary Outcome Results

Percentage of patients achieving an ASAS40 response at Week 24

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.
Time Frame	Baseline, Week 24
Analysis Population Description	Full Analysis Set (FAS): The FAS comprised all patients to whom study treatment/reference treatment was assigned by randomization. Data represent the number of patients with non-missing response at the specified visit.

	Treat-to-Target (T2T)	**Standard-of-care (SOC)**
Arm/Group Description	Treat To Target approach with secukinumab as first line biologic	Patients received treatment according to local practice standards by their treating physician following the current treatment recommendations
Number of Participants Analyzed [units: participants]	144	139
Percentage of patients achieving an ASAS40 response at Week 24 (units: Percentage of participants)		
Week 24	40.1	49.2

Statistical Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 24
Type of Statistical Test	Superiority	
P Value	0.119	

Method	Regression, Logistic
Odds Ratio (OR)	0.69
95 % Confidence Interval 2-Sided	0.43 to 1.10

Secondary Outcome Results

Percentage of patients achieving an ASAS40 response at Week 12

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.
Time Frame	Baseline, Week 12
Analysis Population Description	Full Analysis Set (FAS): The FAS comprised all patients to whom study treatment/reference treatment was assigned by randomization. Data represent the number of patients with non-missing response at the specified visit.

	Treat-to-Target (T2T)	**Standard-of-care (SOC)**
Arm/Group Description	Treat To Target approach with secukinumab as first line biologic	Patients received treatment according to local practice standards by their treating physician following the current treatment recommendations
Number of Participants Analyzed [units: participants]	147	143

Percentage of patients achieving an ASAS40 response at Week 12 (units: Percentage of participants)		
	34.0	46.6

Statistical Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 12
Type of Statistical Test	Superiority	
P Value	0.029	
Method	Regression, Logistic	
Odds Ratio (OR)	0.59	
95 % Confidence Interval 2-Sided	0.37 to 0.95	

Percentage of patients achieving ASAS20 response

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.
Time Frame	Baseline, Weeks 12 and 24
Analysis Population Description	Full Analysis Set (FAS): The FAS comprised all patients to whom study treatment/reference treatment was assigned by randomization. Data represent the number of patients with non-missing response at the specified visit.

	Treat-to-Target (T2T)	Standard-of-care (SOC)
Arm/Group Description	Treat To Target approach with secukinumab as first line biologic	Patients received treatment according to local practice standards by their treating physician following the current treatment recommendations
Number of Participants Analyzed [units: participants]	147	143
Percentage of patients achieving ASAS20 response (units: Percentage of participants)		
Week 12 n=147,143	51.8	60.1
Week 24 n=144,139	62.1	65.3

Statistical Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 12
Type of Statistical Test	Superiority	
P Value	0.154	
Method	Regression, Logistic	
Odds Ratio (OR)	0.71	
95 % Confidence Interval 2-Sided	0.45 to 1.14	

Statistical Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 24
Type of Statistical Test	Superiority	

P Value	0.562
Method	Regression, Logistic
Odds Ratio (OR)	0.87
95 % Confidence Interval 2-Sided	0.54 to 1.39

Percentage of patients achieving ASAS partial remission

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.
Time Frame	Baseline, Weeks 12 and 24
Analysis Population Description	Full Analysis Set (FAS): The FAS comprised all patients to whom study treatment/reference treatment was assigned by randomization. Data represent the number of patients with non-missing response at the specified visit.

	Treat-to-Target (T2T)	**Standard-of-care (SOC)**
Arm/Group Description	Treat To Target approach with secukinumab as first line biologic	Patients received treatment according to local practice standards by their treating physician following the current treatment recommendations
Number of Participants Analyzed [units: participants]	149	143
Percentage of patients achieving ASAS partial remission (units: Percentage of participants)		
Week 12 n=149, 143	18.2	29.0

Week 24 n=146,139	22.8	28.5

Statistical Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 12
Type of Statistical Test	Superiority	
P Value	0.029	
Method	Regression, Logistic	
Odds Ratio (OR)	0.55	
95 % Confidence Interval 2-Sided	0.32 to 0.94	

Statistical Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 24
Type of Statistical Test	Superiority	
P Value	0.264	
Method	Regression, Logistic	
Odds Ratio (OR)	0.74	
95 % Confidence Interval 2-Sided	0.44 to 1.25	

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

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.
Time Frame	Baseline, Weeks 12 and 24
Analysis Population Description	Full Analysis Set (FAS): The FAS comprised all patients to whom study treatment/reference treatment was assigned by randomization. Data represent the number of patients with non-missing response at the specified visit.

	Treat-to-Target (T2T)	Standard-of-care (SOC)
Arm/Group Description	Treat To Target approach with secukinumab as first line biologic	Patients received treatment according to local practice standards by their treating physician following the current treatment recommendations
Number of Participants Analyzed [units: participants]	151	141
Percentage of patients meeting the Ankylosing Spondylitis Disease Activity Score (ASDAS) definition of inactive disease (units: Percentage of participants)		
Week 12 n=151,141	19.8	33.3
Week 24 n=146,136	18.8	33.0

Statistical Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 12
Type of Statistical Test	Superiority	

P Value	0.008
Method	Regression, Logistic
Odds Ratio (OR)	0.49
95 % Confidence Interval 2-Sided	0.29 to 0.83

Statistical Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 24
Type of Statistical Test	Superiority	
P Value	0.005	
Method	Regression, Logistic	
Odds Ratio (OR)	0.47	
95 % Confidence Interval 2-Sided	0.28 to 0.80	

Percentage of patients with ASDAS major improvement

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.
Time Frame	Baseline, Weeks 12 and 24

Analysis Population Description	Full Analysis Set (FAS): The FAS comprised all patients to whom study treatment/reference treatment was assigned by randomization. Data represent the number of patients with non-missing response at the specified visit.

	Treat-to-Target (T2T)	Standard-of-care (SOC)
Arm/Group Description	Treat To Target approach with secukinumab as first line biologic	Patients received treatment according to local practice standards by their treating physician following the current treatment recommendations
Number of Participants Analyzed [units: participants]	151	141
Percentage of patients with ASDAS major improvement (units: Percentage of participants)		
Week 12 n=151,141	19.8	25.6
Week 24 n=146,136	18.6	27.1

Statistical Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 12
Type of Statistical Test	Superiority	
P Value	0.263	
Method	Regression, Logistic	
Odds Ratio (OR)	0.72	
95 % Confidence Interval 2-Sided	0.40 to 1.28	

Statistical Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 24
Type of Statistical Test	Superiority	
P Value	0.103	
Method	Regression, Logistic	
Odds Ratio (OR)	0.61	
95 % Confidence Interval 2-Sided	0.34 to 1.10	

Percentage of patients with ASDAS low disease activity

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.
Time Frame	Baseline, Weeks 12 and 24
Analysis Population Description	Full Analysis Set (FAS): The FAS comprised all patients to whom study treatment/reference treatment was assigned by randomization. Data represent the number of patients with non-missing response at the specified visit.

	Treat-to-Target (T2T)	Standard-of-care (SOC)
Arm/Group Description	Treat To Target approach with secukinumab as first line biologic	Patients received treatment according to local practice standards by their treating physician following the current treatment recommendations

Number of Participants Analyzed [units: participants]	151	141
Percentage of patients with ASDAS low disease activity (units: Percentage of participants)		
Week 12 n=151,141	46.5	57.7
Week 24 n=146,136	52.4	57.2

Statistical Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 12
Type of Statistical Test	Superiority	
P Value	0.055	
Method	Regression, Logistic	
Odds Ratio (OR)	0.64	
95 % Confidence Interval 2-Sided	0.40 to 1.01	

Statistical Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 24
Type of Statistical Test	Superiority	
P Value	0.409	
Method	Regression, Logistic	
Odds Ratio (OR)	0.82	

95 % Confidence Interval 2-Sided	0.52 to 1.31

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

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.
Time Frame	Baseline, Weeks 12 and 24
Analysis Population Description	Full Analysis Set (FAS): The FAS comprised all patients to whom study treatment/reference treatment was assigned by randomization.

	Treat-to-Target (T2T)	Standard-of-care (SOC)
Arm/Group Description	Treat To Target approach with secukinumab as first line biologic	Patients received treatment according to local practice standards by their treating physician following the current treatment recommendations
Number of Participants Analyzed [units: participants]	155	149
Percentage of patients achieving the Bath Ankylosing Spondylitis Disease Activity Index response 50% (BASDAI 50) at Week 12 and Week 24 (units: Percentage of participants)		
Week 12	38.0	42.0
Week 24	42.5	42.2

Statistical Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 12
Type of Statistical Test	Superiority	

P Value	0.477
Method	Regression, Logistic
Odds Ratio (OR)	0.85
95 % Confidence Interval 2-Sided	0.53 to 1.34

Statistical Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 24
Type of Statistical Test	Superiority	
P Value	0.968	
Method	Regression, Logistic	
Odds Ratio (OR)	1.01	
95 % Confidence Interval 2-Sided	0.63 to 1.61	

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

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.
Time Frame	Baseline, Weeks 12 and 24
Analysis Population Description	Full Analysis Set (FAS): The FAS comprised all patients to whom study treatment/reference treatment was assigned by randomization.

	Treat-to-Target (T2T)	Standard-of-care (SOC)
Arm/Group Description	Treat To Target approach with secukinumab as first line biologic	Patients received treatment according to local practice standards by their treating physician following the current treatment recommendations
Number of Participants Analyzed [units: participants]	155	149
Change from Baseline in Bath Ankylosing Spondylitis Functional Index (BASFI) (units: Scores on a scale)	**Least Squares Mean (95% Confidence Interval)**	**Least Squares Mean (95% Confidence Interval)**
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 Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 12
Type of Statistical Test	Superiority	
P Value	0.205	
Method	Regression, Logistic	
Odds Ratio (OR)	0.30	
95 % Confidence Interval 2-Sided	-0.16 to 0.75	

Statistical Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 24
Type of Statistical Test	Superiority	
P Value	0.108	
Method	Regression, Logistic	
Odds Ratio (OR)	0.37	
95 % Confidence Interval 2-Sided	-0.08 to 0.82	

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

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.
Time Frame	Baseline, Weeks 12 and 24
Analysis Population Description	Full Analysis Set (FAS): The FAS comprised all patients to whom study treatment/reference treatment was assigned by randomization.

	Treat-to-Target (T2T)	Standard-of-care (SOC)
Arm/Group Description	Treat To Target approach with secukinumab as first line biologic	Patients received treatment according to local practice standards by their treating physician following the current treatment recommendations
Number of Participants Analyzed [units: participants]	155	149

Change from Baseline in Bath ankylosing spondylitis metrology index (BASMI) (units: Scores on a scale)	**Least Squares Mean** **(95% Confidence Interval)**	**Least Squares Mean** **(95% Confidence Interval)**
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 Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 12
Type of Statistical Test	Superiority	
P Value	0.525	
Method	Mixed Models Analysis	
Mean Difference (Net)	0.06	
95 % Confidence Interval 2-Sided	-0.12 to 0.23	

Statistical Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 24
Type of Statistical Test	Superiority	
P Value	0.577	
Method	Mixed Models Analysis	

Mean Difference (Net)	-0.06
95 % Confidence Interval 2-Sided	-0.25 to 0.14

Change from Baseline in chest expansion

Description	Chest expansion is measured as the cervical rotation angle (in degrees).
Time Frame	Baseline, Weeks 12 and 24
Analysis Population Description	Full Analysis Set (FAS): The FAS comprised all patients to whom study treatment/reference treatment was assigned by randomization.

	Treat-to-Target (T2T)	**Standard-of-care (SOC)**
Arm/Group Description	Treat To Target approach with secukinumab as first line biologic	Patients received treatment according to local practice standards by their treating physician following the current treatment recommendations
Number of Participants Analyzed [units: participants]	155	149
Change from Baseline in chest expansion (units: degrees)	**Least Squares Mean (95% Confidence Interval)**	**Least Squares Mean (95% Confidence Interval)**
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 Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 12
Type of Statistical Test	Superiority	

P Value	0.220
Method	Mixed Models Analysis
Odds Ratio (OR)	-0.89
95 % Confidence Interval 2-Sided	-2.32 to 0.54

Statistical Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 24
Type of Statistical Test	Superiority	
P Value	0.745	
Method	Regression, Logistic	
Median Difference (Net)	-0.10	
95 % Confidence Interval 2-Sided	-0.70 to 0.50	

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

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.
Time Frame	Baseline, Weeks 12 and 24
Analysis Population Description	Full Analysis Set (FAS): The FAS comprised all patients to whom study treatment/reference treatment was assigned by randomization.

	Treat-to-Target (T2T)	Standard-of-care (SOC)
Arm/Group Description	Treat To Target approach with secukinumab as first line biologic	Patients received treatment according to local practice standards by their treating physician following the current treatment recommendations
Number of Participants Analyzed [units: participants]	155	149
Change from Baseline in the ASQoL (Ankylosing Spondylitis Quality of Life instrument) (units: Scores on a scale)	**Least Squares Mean (95% Confidence Interval)**	**Least Squares Mean (95% Confidence Interval)**
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 Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 12
Type of Statistical Test	Superiority	
P Value	0.768	
Method	Mixed Models Analysis	
Mean Difference (Net)	-0.13	
95 % Confidence Interval 2-Sided	-1.01 to 0.74	

Statistical Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 24
Type of Statistical Test	Superiority	
P Value	0.451	
Method	Mixed Models Analysis	
Mean Difference (Net)	-0.37	
95 % Confidence Interval 2-Sided	-1.34 to 0.60	

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

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.
Time Frame	Baseline, Weeks 12 and 24
Analysis Population Description	Full Analysis Set (FAS): The FAS comprised all patients to whom study treatment/reference treatment was assigned by randomization.

	Treat-to-Target (T2T)	Standard-of-care (SOC)
Arm/Group Description	Treat To Target approach with secukinumab as first line biologic	Patients received treatment according to local practice standards by their treating physician following the current treatment recommendations

Number of Participants Analyzed [units: participants]	155	149
Change from Baseline in ASAS-HI (Ankylosing Spondyloarthritis International Society Health Index) (units: Scores on a scale)	**Least Squares Mean (95% Confidence Interval)**	**Least Squares Mean (95% Confidence Interval)**
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 Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 12
Type of Statistical Test	Superiority	
P Value	0.477	
Method	Mixed Models Analysis	
Mean Difference (Net)	0.26	
95 % Confidence Interval 2-Sided	-0.46 to 0.97	

Statistical Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 24
Type of Statistical Test	Superiority	
P Value	0.660	
Method	Mixed Models Analysis	

Mean Difference (Net)	-0.17
95 % Confidence Interval 2-Sided	-0.92 to 0.58

Change from Baseline in global disease assessment (patient)

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.
Time Frame	Baseline, Weeks 12 and 24
Analysis Population Description	Full Analysis Set (FAS): The FAS comprised all patients to whom study treatment/reference treatment was assigned by randomization.

	Treat-to-Target (T2T)	**Standard-of-care (SOC)**
Arm/Group Description	Treat To Target approach with secukinumab as first line biologic	Patients received treatment according to local practice standards by their treating physician following the current treatment recommendations
Number of Participants Analyzed [units: participants]	155	149
Change from Baseline in global disease assessment (patient) (units: Scores on a scale)	**Least Squares Mean (95% Confidence Interval)**	**Least Squares Mean (95% Confidence Interval)**
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 Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 12

Type of Statistical Test	Superiority
P Value	0.586
Method	Mixed Models Analysis
Mean Difference (Net)	0.17
95 % Confidence Interval 2-Sided	-0.45 to 0.79

Statistical Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 24
Type of Statistical Test	Superiority	
P Value	0.491	
Method	Mixed Models Analysis	
Median Difference (Net)	0.21	
95 % Confidence Interval 2-Sided	-0.39 to 0.82	

Change from Baseline in global disease assessment (physician)

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.
Time Frame	Baseline, Weeks 12 and 24

Analysis Population Description	Full Analysis Set (FAS): The FAS comprised all patients to whom study treatment/reference treatment was assigned by randomization.

	Treat-to-Target (T2T)	**Standard-of-care (SOC)**
Arm/Group Description	Treat To Target approach with secukinumab as first line biologic	Patients received treatment according to local practice standards by their treating physician following the current treatment recommendations
Number of Participants Analyzed [units: participants]	155	149
Change from Baseline in global disease assessment (physician) (units: Scores on a scale)	**Least Squares Mean (90% Confidence Interval)**	**Least Squares Mean (90% Confidence Interval)**
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 Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)
Type of Statistical Test	Superiority
Non-Inferiority/Equivalence Test	Week 12
P Value	0.082
Method	Mixed Models Analysis
Mean Difference (Net)	4.49

95 % Confidence Interval 2-Sided	-0.58 to 9.56

Statistical Analysis

Groups	Treat-to-Target (T2T), Standard-of-care (SOC)	Week 24
Type of Statistical Test	Superiority	
P Value	0.292	
Method	Mixed Models Analysis	
Median Difference (Net)	2.73	
95 % Confidence Interval 2-Sided	-2.35 to 7.81	

Safety Results

Time Frame	Adverse Events (AEs) were reported from first dose of study treatment until end of study treatment plus 20 weeks up to approximately 56 weeks.
Additional Description	The safety set included all patients who received at least one dose of study treatment. AEs are reported according to the actual treatment received when AE started. As Secukinumab 150 mg could also had been provided in the Standard-of-Care arm, the number of patients at risk exceeds the number of patients enrolled in the T2T arm. For AEs that occurred while on other treatment in the SoC arm, the specific treatment information was not collected, and AEs summarized under one arm.
Source Vocabulary for Table Default	MedDRA (25.1)

Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	Secukinumab 150 mg N = 190	Secukinumab 300 mg N = 92	Adalimumab 40 mg N = 116	Other Treatment N = 128	Overall N = 303
Arm/Group Description	Secukinumab 150 mg	Secukinumab 300 mg	Adalimumab 40 mg	Other treatment included concomitant and rescue medications other than study drugs.	Overall
Total Number Affected	0	0	0	0	0
Total Number At Risk	190	92	116	128	303

Serious Adverse Events

Time Frame	Adverse Events (AEs) were reported from first dose of study treatment until end of study treatment plus 20 weeks up to approximately 56 weeks.
Additional Description	The safety set included all patients who received at least one dose of study treatment. AEs are reported according to the actual treatment received when AE started. As Secukinumab 150 mg could also had been provided in the Standard-of-Care arm, the number of patients at risk exceeds the number of patients enrolled in the T2T arm. For AEs that occurred while on other treatment in the SoC arm, the specific treatment information was not collected, and AEs summarized under one arm.
Source Vocabulary for Table Default	MedDRA (25.1)

Collection Approach for Table Default Systematic Assessment

	Secukinumab 150 mg N = 190	Secukinumab 300 mg N = 92	Adalimumab 40 mg N = 116	Other Treatment N = 128	Overall N = 303
Arm/Group Description	Secukinumab 150 mg	Secukinumab 300 mg	Adalimumab 40 mg	Other treatment included concomitant and rescue medications other than study drugs.	Overall
Total # Affected by any Serious Adverse Event	10	4	5	8	16
Total # at Risk by any Serious Adverse Event	190	92	116	128	303
Cardiac disorders					
Angina pectoris	1 (0.53%)	1 (1.09%)	0 (0.00%)	0 (0.00%)	1 (0.33%)
Coronary artery disease	1 (0.53%)	1 (1.09%)	0 (0.00%)	0 (0.00%)	1 (0.33%)
Tachycardia	1 (0.53%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.33%)
Gastrointestinal disorders					
Diarrhoea haemorrhagic	1 (0.53%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.33%)
Immune system disorders					
Immunisation reaction	1 (0.53%)	0 (0.00%)	1 (0.86%)	0 (0.00%)	1 (0.33%)
Injury, poisoning and procedural complications					
Muscle strain	1 (0.53%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.33%)

Radius fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.78%)	1 (0.33%)
Scapula fracture	0 (0.00%)	0 (0.00%)	1 (0.86%)	1 (0.78%)	1 (0.33%)
Musculoskeletal and connective tissue disorders					
Ankylosing spondylitis	2 (1.05%)	0 (0.00%)	1 (0.86%)	2 (1.56%)	2 (0.66%)
Osteoarthritis	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.78%)	1 (0.33%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)					
Basal cell carcinoma	1 (0.53%)	1 (1.09%)	0 (0.00%)	0 (0.00%)	1 (0.33%)
Fibroadenoma of breast	0 (0.00%)	0 (0.00%)	1 (0.86%)	1 (0.78%)	1 (0.33%)
Nervous system disorders					
Sciatica	0 (0.00%)	0 (0.00%)	1 (0.86%)	1 (0.78%)	1 (0.33%)
Pregnancy, puerperium and perinatal conditions					
Abortion spontaneous	1 (0.53%)	1 (1.09%)	0 (0.00%)	0 (0.00%)	1 (0.33%)
Skin and subcutaneous tissue disorders					
Dermatitis atopic	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.78%)	1 (0.33%)

Other (Not Including Serious) Adverse Events

Time Frame	Adverse Events (AEs) were reported from first dose of study treatment until end of study treatment plus 20 weeks up to approximately 56 weeks.
Additional Description	The safety set included all patients who received at least one dose of study treatment. AEs are reported according to the actual treatment received when AE started. As Secukinumab 150 mg could also had been provided in the Standard-of-Care arm, the number

	of patients at risk exceeds the number of patients enrolled in the T2T arm. For AEs that occurred while on other treatment in the SoC arm, the specific treatment information was not collected, and AEs summarized under one arm.
Source Vocabulary for Table Default	MedDRA (25.1)
Collection Approach for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	5%

	Secukinumab 150 mg N = 190	**Secukinumab 300 mg N = 92**	**Adalimumab 40 mg N = 116**	**Other Treatment N = 128**	**Overall N = 303**
Arm/Group Description	Secukinumab 150 mg	Secukinumab 300 mg	Adalimumab 40 mg	Other treatment included concomitant and rescue medications other than study drugs.	Overall
Total # Affected by any Other Adverse Event	69	38	35	36	98
Total # at Risk by any Other Adverse Event	190	92	116	128	303
Gastrointestinal disorders					
Diarrhoea	16 (8.42%)	9 (9.78%)	8 (6.90%)	11 (8.59%)	24 (7.92%)
Nausea	12 (6.32%)	6 (6.52%)	3 (2.59%)	7 (5.47%)	14 (4.62%)
General disorders and administration site conditions					
Fatigue	7 (3.68%)	3 (3.26%)	6 (5.17%)	5 (3.91%)	12 (3.96%)

Infections and infestations					
Nasopharyngitis	24 (12.63%)	13 (14.13%)	7 (6.03%)	10 (7.81%)	31 (10.23%)
Respiratory tract infection	10 (5.26%)	3 (3.26%)	3 (2.59%)	3 (2.34%)	10 (3.30%)
Upper respiratory tract infection	10 (5.26%)	6 (6.52%)	6 (5.17%)	3 (2.34%)	12 (3.96%)
Musculoskeletal and connective tissue disorders					
Arthralgia	7 (3.68%)	6 (6.52%)	3 (2.59%)	0 (0.00%)	8 (2.64%)
Nervous system disorders					
Headache	12 (6.32%)	7 (7.61%)	7 (6.03%)	6 (4.69%)	18 (5.94%)

Other Relevant Findings

None

Conclusion:

The study failed to demonstrate the superiority of efficacy with the T2T approach over the SOC. Besides, most of the efficacy outcomes were similar between the T2T approach and the SOC. Further studies would be required to address the research question of optimal treatment strategy in the current study population.

Date of Clinical Trial Report

08 August 2023