NOVARTIS

Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Secukinumab

Trial Indication(s)

Active Ankylosing Spondylitis

Protocol Number

CAIN457F2310

Protocol Title

A randomized, double-blind, placebo-controlled phase III study of subcutaneous secukinumab in prefilled syringes to demonstrate efficacy at 16 weeks and to assess long-term efficacy, safety and tolerability up to 5 years in patients with active Ankylosing Spondylitis

Clinical Trial Phase

Phase 3

Phase of Drug Development

Phase III

Study Start/End Dates

Study Start Date: October 2012 (Actual)
Primary Completion Date: September 2018 (Actual)
Study Completion Date: September 2018 (Actual)

Reason for Termination (If applicable)

Study Design/Methodology

This was a pivotal phase III study using a double-blind, randomized, parallel-group, double-dummy, placebo-controlled design in patients with ankylosing spondylitis. A screening period running 4-10 weeks before randomization was used to assess eligibility, followed by a treatment period of 52 weeks of blinded treatment. At baseline (BSL),:

- Group 1: secukinumab 75 mg plus placebo 150 mg once weekly at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4
- Group 2: secukinumab 150 mg plus placebo 75 mg once weekly at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4
- Group 3: placebo 75 mg and placebo 150 mg once weekly at BSL, Weeks 1, 2, 3 and 4, followed by dosing every four weeks starting at Week 4

The patients were stratified at randomization according to prior TNFα-inhibitor exposure: approximately 40% of randomized patients were required to be TNFα-IR in order to evaluate the efficacy and safety in this patient population.

At Week 16, patients who had been randomized to placebo at baseline were re-randomized to receive secukinumab 75 mg plus placebo 150 mg or secukinumab 150 mg plus placebo 75 mg (1:1) every 4 weeks up to 256 weeks.

After Week 52 site personnel and the patient were unblinded to the patient's treatment regimen in order to eliminate the placebo injection. After implementation of the Amendment 2, the study medication for patients on the 75 mg treatment arm could be escalated from 75 mg to 150 mg every 4 weeks for patients whose overall therapeutic response was not fully achieved and might improve with a higher dose, as judged by the investigator.

Centers

54 centers in 13 countries: United States(11), Netherlands(2), Italy(3), United Kingdom(4), Spain(4), Czech Republic(4), Switzerland(3), Canada(4), Austria(2), Germany(3), Finland(5), Russia(7), Singapore(2)

Objectives:

The primary objective of this study was to demonstrate that the efficacy of secukinumab 75 mg sc or 150 mg sc at Week 16 was superior to placebo in patients with active AS based on the proportion of patients achieving an ASAS20 (Assessment of SpondyloArthritis International Society criteria) response.

The secondary objectives were to demonstrate that the efficacy of at least one dose of secukinumab at Week 16 was superior to placebo in patients with active AS based on the following endpoints:

- the proportion of patients achieving an ASAS40 response
- the change from baseline in high-sensitivity C-reactive protein (hsCRP)
- the proportion of patients achieving an ASAS 5/6 response
- the change from baseline in total Bath Ankylosing Spondylitis Disease Activity (BASDAI)
- the change from baseline in SF-36 physical component summary (SF-36 PCS)
- the change from baseline in Ankylosing Spondylitis Quality of Life (ASQoL)
- the proportion of patients achieving an ASAS partial remission

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

Secukinumab 75 mg/150 mg provided in 0.5/1.0 ml prefilled syringe (PFS) for subcutaneous (s.c) injection.

Statistical Methods

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).

Comparative primary efficacy analyses (i.e. inferential efficacy comparisons with placebo) focuses on data until Week 16 (time period when both active drug and the placebo are given in a manner suitable for making comparisons (e.g. double-blind)).

A sequentially rejective 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%, adjusting for multiplicity of testing across the doses and endpoints.

The primary efficacy variable was the response to treatment according to the ASAS 20 criteria at Week 16, defined as an improvement of ≥20% and ≥1 unit on a scale of 0-10 in at least three of the four main domains and no worsening of ≥20% and ≥1 unit on a scale of 0-10 in the remaining domain. The statistical hypothesis for ASAS 20 being tested was that there was no difference in the proportion of patients fulfilling the ASAS 20 criteria at Week 16 in any of the secukinumab regimens versus the placebo regimen. The primary analysis was conducted via logistic regression with treatment and TNF-α inhibitor status as factors and weight as a covariate. Odds ratios and 95% CI were presented comparing each secukinumab regimen to placebo. A sensitivity analysis to determine the robustness of the logistic regression model was performed using a non-parametric ANCOVA model with the same independent variables as the logistic regression model. The impact of missing data on the analysis results of ASAS 20 response was assessed as well by repeating the logistic regression model using multiple imputation and observed data analysis to handle missing data.

For the continuous secondary efficacy variables, between-treatment differences in the change from baseline in hsCRP, total BASDAI, SF-36 PCS and ASQoL were evaluated using a mixed-effect model repeated measures (MMRM) model with treatment group, analysis visit, and TNF-α inhibitor status as factors and, as continuous covariates, the baseline value and weight. Treatment by analysis visit and the baseline value by analysis visit were included as interaction terms in the model. An unstructured covariance structure was assumed for the MMRM model.

For the binary secondary efficacy variables, the proportion of patients meeting the ASAS 40 (defined as an improvement of ≥40% and ≥2 units on a scale of 0-10 in at least three of the four main domains and no worsening at all in the remaining domain), the ASAS 5/6 improvement criteria (defined as an improvement of ≥20% in at least five domains) or the ASAS partial remission criteria (defined as a value not above 2 units in each of the 4 core ASAS domains on a scale of 0-10) was evaluated using a logistic regression model with treatment and TNF-α inhibitor status as factors and weight as a covariate.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:
- Male or non-pregnant, non-lactating female patients
- Diagnosis of moderate to severe AS with prior documented radiologic evidence (x-ray) fulfilling the Modified New York criteria for AS (1984)
- Patients should have been on NSAIDs with an inadequate response
- Patients who were regularly taking NSAIDs as part of their AS therapy are required to be on a stable dose
- Patients who had been on an anti-TNFα agent (not more than one) must have experienced an inadequate response

Exclusion Criteria:
- Chest X-ray (or MRI) with evidence of ongoing infectious or malignant process

- Patients with total ankylosis of the spine
- Patients previously treated with any biological immunomodulating agents except for those targeting TNFα
- Previous treatment with any cell-depleting therapies

Participant Flow Table

Up to Week 16

	Secukinumab 75 mg	Secukinumab 150 mg	Placebo	Placebo - secukinumab 75 mg	Placebo - secukinumab 150 mg	Total
Arm/Group Description	Secukinumab 75 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks.	Secukinumab 150 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks	Placebo subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks up to week 16	Placebo patients re-randomized to secukinumab 75 mg subcutaneous injection every 4 weeks starting from week 16.	Placebo patients re-randomized to secukinumab 150 mg subcutaneous injection every 4 weeks starting from week 16.	
Started	73	72	74	0	0	219
Completed	68	66	66	0	0	200
Not Completed	5	6	8	0	0	19
Adverse Event	2	5	4	0	0	11
Lack of Efficacy	0	0	1	0	0	1
Physician Decision	0	0	1	0	0	1
Withdrawal by Subject	2	1	2	0	0	5
Death	1	0	0	0	0	1

Week 16 up to Week 260

	Secukinumab 75 mg	Secukinumab 150 mg	Placebo	Placebo - secukinumab 75 mg	Placebo - secukinumab 150 mg	Total
Arm/Group Description	Secukinumab 75 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks.	Secukinumab 150 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks	Placebo subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks up to week 16	Placebo patients re-randomized to secukinumab 75 mg subcutaneous injection every 4 weeks starting from week 16.	Placebo patients re-randomized to secukinumab 150 mg subcutaneous injection every 4 weeks starting from week 16.	
Started	68	66	0	32	34	200
Completed	48	53	0	20	29	150
Not Completed	20	13	0	12	5	50
Lack of Efficacy	7	4	0	4	2	17
Non-compliance	0	1	0	1	0	2
Physician Decision	0	2	0	0	0	2
Technical issues	0	1	0	1	0	2
Withdrawal by Subject	7	2	0	3	1	13
Death	1	1	0	0	0	2
Adverse Event	5	2	0	3	2	12

Baseline Characteristics

	Secukinumab 75 mg	Secukinumab 150 mg	Placebo	Total
Arm/Group Description	Secukinumab 75 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks.	Secukinumab 150 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks	Placebo subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks up to week 16	
Number of Participants [units: participants]	73	72	74	219
Age, Customized (units: participants)				
< 65	70	70	72	212
>= 65 to 74	2	2	1	5
>= 75	1	0	1	2
Sex: Female, Male (units:) Count of Participants (Not Applicable)				
Female	22	26	18	66
Male	51	46	56	153
Race/Ethnicity, Customized (units: participants)				
White	70	69	70	209
Asian	3	2	4	9

American Indian or Alaska Native	0	1	0	1

Summary of Efficacy

Primary Outcome Result(s)

Percentage of participants achieving ASAS 20 (SpondyloArthritis International Society criteria) response at week 16

(Time Frame: Baseline up to 16 weeks)

	Secukinumab 75 mg	Secukinumab 150 mg	Placebo
Arm/Group Description	Secukinumab 75 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks.	Secukinumab 150 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks	Placebo subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks up to week 16
Number of Participants Analyzed [units: participants]	73	72	74
Percentage of participants achieving ASAS 20 (SpondyloArthritis International Society criteria) response at week 16 (units: percentage of			

participants)			
n=30,44,21	41.1	61.1	28.4

Statistical Analysis

Groups	Secukinumab 75 mg, Placebo	
P Value	0.0967	
Method	Regression, Logistic	Missing ASAS responses considered nonresponders
Odds Ratio (OR)	1.82	
95 % Confidence Interval 2-Sided	0.90 to 3.67	

Statistical Analysis

Groups	Secukinumab 150 mg, Placebo	
P Value	<.0001	
Method	Regression, Logistic	Missing ASAS responses considered nonresponders
Odds Ratio (OR)	4.38	
95 % Confidence Interval 2-Sided	2.14 to 8.96	

Secondary Outcome Result(s)

Percentage of participants achieving ASAS 40 (SpondyloArthritis International Society criteria) response

(Time Frame: Baseline up to 16 weeks)

	Secukinumab 75 mg	Secukinumab 150 mg	Placebo
Arm/Group Description	Secukinumab 75 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks.	Secukinumab 150 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks	Placebo subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks up to week 16
Number of Participants Analyzed [units: participants]	73	72	74
Percentage of participants achieving ASAS 40 (SpondyloArthritis International Society criteria) response (units: percentage of participants)			
n=19,26,8	26.0	36.1	10.8

Statistical Analysis

Groups	Secukinumab 75 mg, Placebo
P Value	0.0194

Method	Regression, Logistic	Missing ASAS responses considered nonresponders
Odds Ratio (OR)	2.99	
95 % Confidence Interval 2-Sided	1.19 to 7.48	

Statistical Analysis

Groups	Secukinumab 150 mg, Placebo	
P Value	<.0004	
Method	Regression, Logistic	Missing ASAS responses considered nonresponders
Odds Ratio (OR)	5.07	
95 % Confidence Interval 2-Sided	2.06 to 12.44	

Change from baseline at week 16 in serum hsCRP

(Time Frame: 16 weeks)

	Secukinumab 75 mg	**Secukinumab 150 mg**	**Placebo**
Arm/Group Description	Secukinumab 75 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks.	Secukinumab 150 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks	Placebo subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks up to week 16

Number of Participants Analyzed [units: participants]	73	72	74
Change from baseline at week 16 in serum hsCRP (units: mg/L) Least Squares Mean ± Standard Error			
n=69,68,66	0.61 ± 1.103	0.55 ± 1.104	1.13 ± 1.105

Statistical Analysis

Groups	Secukinumab 75 mg, Placebo
P Value	<0.0001
Method	Mixed Models Analysis
Mean Difference (Net)	0.54
95 % Confidence Interval 2-Sided	0.41 to 0.71

Statistical Analysis

Groups	Secukinumab 150 mg, Placebo
P Value	<0.0001
Method	Mixed Models Analysis
Mean Difference (Net)	0.49

95 % Confidence Interval 2-Sided	0.37 to 0.64

Percentage of participants achieving ASAS 5/6 (SpondyloArthritis International Society criteria) response at week 16

(Time Frame: Baseline up to 16 weeks)

	Secukinumab 75 mg	Secukinumab 150 mg	Placebo
Arm/Group Description	Secukinumab 75 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks.	Secukinumab 150 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks	Placebo subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks up to week 16
Number of Participants Analyzed [units: participants]	73	72	74
Percentage of participants achieving ASAS 5/6 (SpondyloArthritis International Society criteria) response at week 16 (units: percentage of participants)			
n=25,31,6	34.2	43.1	8.1

Statistical Analysis

Groups	Secukinumab 75 mg, Placebo

P Value	0.0003	
Method	Regression, Logistic	Missing ASAS responses considered nonresponders
Odds Ratio (OR)	6.13	
95 % Confidence Interval 2-Sided	2.31 to 16.26	

Statistical Analysis

Groups	Secukinumab 150 mg, Placebo	
P Value	<.0001	
Method	Regression, Logistic	Missing ASAS responses considered nonresponders
Odds Ratio (OR)	9.15	
95 % Confidence Interval 2-Sided	3.47 to 24.12	

Change from baseline at week 16 for total Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

(Time Frame: Baseline up to 16 weeks)

	Secukinumab 75 mg	Secukinumab 150 mg	Placebo
Arm/Group Description	Secukinumab 75 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by	Secukinumab 150 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by	Placebo subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every

	dosing every 4 weeks.	dosing every 4 weeks	4 weeks up to week 16
Number of Participants Analyzed [units: participants]	73	72	74
Change from baseline at week 16 for total Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) (units: scores on a scale) Least Squares Mean ± Standard Error			
n=67,67,64	-1.92 ± 0.249	-2.19 ± 0.248	-0.85 ± 0.252

Statistical Analysis

Groups	Secukinumab 75 mg, Placebo
P Value	<0.0001
Method	Mixed Models Analysis
Mean Difference (Net)	-1.07
Standard Error of the mean	0.353
95 % Confidence Interval 2-Sided	-1.77 to -0.37

Statistical Analysis

Groups	Secukinumab 150 mg, Placebo
P Value	0.0002

Method	Mixed Models Analysis
Mean Difference (Net)	-1.34
Standard Error of the mean	0.353
95 % Confidence Interval 2-Sided	-2.04 to -0.65

Change from baseline at week 16 in Physical Function Component Summary (PCS) of the Medical Outcomes Study Questionnaire Short-form Health Survey (SF-36)

(Time Frame: Baseline up to 16 weeks)

	Secukinumab 75 mg	Secukinumab 150 mg	Placebo
Arm/Group Description	Secukinumab 75 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks.	Secukinumab 150 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks	Placebo subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks up to week 16
Number of Participants Analyzed [units: participants]	73	72	74
Change from baseline at week 16 in Physical Function Component Summary (PCS) of the Medical Outcomes Study Questionnaire Short-form Health Survey (SF-36) (units: scores on a scale)			

Least Squares Mean ± Standard Error			
n=66,67,66	4.77 ± 0.798	6.06 ± 0.784	1.92 ± 0.786

Statistical Analysis

Groups	Secukinumab 75 mg, Placebo
P Value	0.0110
Method	Mixed Models Analysis
Mean Difference (Net)	2.84
Standard Error of the mean	1.108
95 % Confidence Interval 2-Sided	0.66 to 5.03

Statistical Analysis

Groups	Secukinumab 150 mg, Placebo
P Value	0.0002
Method	Mixed Models Analysis
Mean Difference (Net)	4.14
Standard Error of the mean	1.105
95 % Confidence Interval 2-Sided	1.96 to 6.32

Change from baseline at week 16 in ASQoL

(Time Frame: Baseline up to 16 weeks)

	Secukinumab 75 mg	Secukinumab 150 mg	Placebo
Arm/Group Description	Secukinumab 75 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks.	Secukinumab 150 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks	Placebo subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks up to week 16
Number of Participants Analyzed [units: participants]	73	72	74
Change from baseline at week 16 in ASQoL (units: scores on a scale) Least Squares Mean ± Standard Error			
n=66,66,66	-3.33 ± 0.537	-4.00 ± 0.528	-1.37 ± 0.530

Statistical Analysis

Groups	Secukinumab 75 mg, Placebo
P Value	0.0096
Method	Mixed Models Analysis
Mean Difference (Net)	-1.96

Standard Error of the mean	0.748
95 % Confidence Interval 2-Sided	-3.43 to -0.48

Statistical Analysis

Groups	Secukinumab 150 mg, Placebo
P Value	0.0005
Method	Mixed Models Analysis
Mean Difference (Net)	-2.63
Standard Error of the mean	0.743
95 % Confidence Interval 2-Sided	-4.09 to -1.16

Percentage of participants achieving ASAS partial remission at week 16

(Time Frame: Baseline up to 16 weeks)

	Secukinumab 75 mg	**Secukinumab 150 mg**	**Placebo**
Arm/Group Description	Secukinumab 75 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks.	Secukinumab 150 mg subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks	Placebo subcutaneous injection once weekly at baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks up to week 16

Number of Participants Analyzed [units: participants]	73	72	74
Percentage of participants achieving ASAS partial remission at week 16 (units: percentage of participants)			
n=11,10,3	15.1	13.9	4.1

Statistical Analysis

Groups	Secukinumab 75 mg, Placebo	
P Value	0.0325	
Method	Regression, Logistic	Missing ASAS responses considered nonresponders
Odds Ratio (OR)	4.28	
95 % Confidence Interval 2-Sided	1.13 to 16.21	

Statistical Analysis

Groups	Secukinumab 150 mg, Placebo	
P Value	0.0471	
Method	Regression, Logistic	Missing ASAS responses considered nonresponders
Odds Ratio (OR)	3.91	

95 % Confidence Interval 2-Sided	1.02 to 15.01

Summary of Safety

Safety Results

All-Cause Mortality

	Any secukinumab 75 mg N = 105	Any secukinumab 150 mg N = 155	Placebo N = 74
Arm/Group Description	Includes patients originally randomized to secukinumab 75 mg at baseline and placebo patients who were re-randomized to secukinumab 75 mg at week 16 (AEs occurring after re-randomization).	Includes patients originally randomized to secukinumab 150 mg at baseline, placebo patients re-randomized to secukinumab 150 mg at Week 16 (AEs occuring after re-randomization) and patients who up-titrated from secukinumab	Includes patients originally randomized to Placebo for AEs until the time of re-randomization (Week 16) to Secukinumab

		75 mg to 150 mg (AEs occurring after up-titration).	
Total participants affected	2 (1.90%)	1 (0.65%)	0 (0.00%)

Serious Adverse Events by System Organ Class

Time Frame	Adverse Events and Serious Adverse Events were collected for the maximum actual duration of treatment exposure and follow up for a participant per the protocol for approximately up to 5.5 years
Source Vocabulary for Table Default	MedDRA (21.0)
Assessment Type for Table Default	Systematic Assessment

	Any secukinumab 75 mg N = 105	**Any secukinumab 150 mg N = 155**	**Placebo N = 74**
Arm/Group Description	Includes patients originally randomized to secukinumab 75 mg at baseline and placebo patients who were re-randomized to secukinumab 75 mg at week 16 (AEs occurring after	Includes patients originally randomized to secukinumab 150 mg at baseline, placebo patients re-randomized to secukinumab 150 mg at Week 16 (AEs occuring after re-randomization)	Includes patients originally randomized to Placebo for AEs until the time of re-randomization (Week 16) to Secukinumab

	re-randomization).	and patients who up-titrated from secukinumab 75 mg to 150 mg (AEs occurring after up-titration).	
Total participants affected	25 (23.81%)	31 (20.00%)	4 (5.41%)
Blood and lymphatic system disorders			
Iron deficiency anaemia	1 (0.95%)	0 (0.00%)	0 (0.00%)
Cardiac disorders			
Acute coronary syndrome	1 (0.95%)	0 (0.00%)	0 (0.00%)
Acute myocardial infarction	0 (0.00%)	1 (0.65%)	0 (0.00%)
Angina pectoris	0 (0.00%)	1 (0.65%)	0 (0.00%)
Atrioventricular block complete	0 (0.00%)	1 (0.65%)	0 (0.00%)
Coronary artery stenosis	0 (0.00%)	1 (0.65%)	0 (0.00%)
Myocardial infarction	2 (1.90%)	1 (0.65%)	0 (0.00%)
Eye disorders			
Iridocyclitis	1 (0.95%)	0 (0.00%)	0 (0.00%)
Iritis	0 (0.00%)	1 (0.65%)	0 (0.00%)
Gastrointestinal disorders			
Abdominal hernia	1 (0.95%)	0 (0.00%)	0 (0.00%)
Abdominal pain upper	0 (0.00%)	1 (0.65%)	0 (0.00%)

Anal fissure	0 (0.00%)	1 (0.65%)	0 (0.00%)
Colitis ischaemic	1 (0.95%)	0 (0.00%)	0 (0.00%)
Colitis microscopic	1 (0.95%)	0 (0.00%)	0 (0.00%)
Colitis ulcerative	1 (0.95%)	1 (0.65%)	0 (0.00%)
Crohn's disease	2 (1.90%)	2 (1.29%)	0 (0.00%)
Diarrhoea	0 (0.00%)	1 (0.65%)	0 (0.00%)
Incarcerated hiatus hernia	1 (0.95%)	0 (0.00%)	0 (0.00%)
General disorders and administration site conditions			
Drug ineffective	1 (0.95%)	0 (0.00%)	0 (0.00%)
Hepatobiliary disorders			
Cholecystitis acute	0 (0.00%)	1 (0.65%)	0 (0.00%)
Cholelithiasis	0 (0.00%)	1 (0.65%)	0 (0.00%)
Immune system disorders			
Sarcoidosis	0 (0.00%)	1 (0.65%)	0 (0.00%)
Infections and infestations			
Anal abscess	1 (0.95%)	0 (0.00%)	0 (0.00%)
Arthritis bacterial	0 (0.00%)	1 (0.65%)	0 (0.00%)
Erysipelas	1 (0.95%)	0 (0.00%)	0 (0.00%)
Febrile infection	0 (0.00%)	1 (0.65%)	0 (0.00%)
Gallbladder abscess	0 (0.00%)	1 (0.65%)	0 (0.00%)
Gastroenteritis salmonella	0 (0.00%)	1 (0.65%)	0 (0.00%)
Groin abscess	1 (0.95%)	0 (0.00%)	0 (0.00%)

Influenza	1 (0.95%)	0 (0.00%)	0 (0.00%)
Meningitis viral	1 (0.95%)	0 (0.00%)	0 (0.00%)
Pharyngitis	1 (0.95%)	0 (0.00%)	0 (0.00%)
Pneumonia	2 (1.90%)	2 (1.29%)	0 (0.00%)
Postoperative wound infection	1 (0.95%)	0 (0.00%)	0 (0.00%)
Injury, poisoning and procedural complications			
Concussion	0 (0.00%)	0 (0.00%)	1 (1.35%)
Hip fracture	0 (0.00%)	1 (0.65%)	0 (0.00%)
Lower limb fracture	1 (0.95%)	0 (0.00%)	0 (0.00%)
Lumbar vertebral fracture	1 (0.95%)	0 (0.00%)	0 (0.00%)
Multiple injuries	0 (0.00%)	1 (0.65%)	0 (0.00%)
Rib fracture	1 (0.95%)	0 (0.00%)	0 (0.00%)
Spinal compression fracture	1 (0.95%)	0 (0.00%)	0 (0.00%)
Spinal cord injury cervical	1 (0.95%)	0 (0.00%)	0 (0.00%)
Splenic rupture	1 (0.95%)	0 (0.00%)	0 (0.00%)
Investigations			
Hepatic enzyme increased	0 (0.00%)	1 (0.65%)	0 (0.00%)
Musculoskeletal and connective tissue disorders			
Ankylosing spondylitis	1 (0.95%)	0 (0.00%)	0 (0.00%)
Arthritis	0 (0.00%)	0 (0.00%)	1 (1.35%)

Back pain	1 (0.95%)	0 (0.00%)	0 (0.00%)
Costochondritis	0 (0.00%)	1 (0.65%)	0 (0.00%)
Foot deformity	0 (0.00%)	1 (0.65%)	0 (0.00%)
Intervertebral disc protrusion	0 (0.00%)	1 (0.65%)	1 (1.35%)
Osteoarthritis	1 (0.95%)	1 (0.65%)	0 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Glioblastoma	0 (0.00%)	1 (0.65%)	0 (0.00%)
Intraductal proliferative breast lesion	1 (0.95%)	0 (0.00%)	0 (0.00%)
Malignant melanoma	0 (0.00%)	1 (0.65%)	0 (0.00%)
Paraganglion neoplasm	0 (0.00%)	1 (0.65%)	0 (0.00%)
Superficial spreading melanoma stage unspecified	0 (0.00%)	0 (0.00%)	1 (1.35%)
Nervous system disorders			
Carpal tunnel syndrome	1 (0.95%)	0 (0.00%)	0 (0.00%)
Headache	0 (0.00%)	2 (1.29%)	0 (0.00%)
Ischaemic stroke	0 (0.00%)	2 (1.29%)	0 (0.00%)
Quadriparesis	0 (0.00%)	1 (0.65%)	0 (0.00%)
Quadriplegia	1 (0.95%)	0 (0.00%)	0 (0.00%)
Transient ischaemic attack	0 (0.00%)	1 (0.65%)	0 (0.00%)
Psychiatric disorders			
Depression	0 (0.00%)	0 (0.00%)	1 (1.35%)

Renal and urinary disorders			
Nephrotic syndrome	1 (0.95%)	0 (0.00%)	0 (0.00%)
Stress urinary incontinence	0 (0.00%)	1 (0.65%)	0 (0.00%)
Reproductive system and breast disorders			
Vaginal haemorrhage	1 (0.95%)	0 (0.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders			
Nasal septum deviation	0 (0.00%)	1 (0.65%)	0 (0.00%)
Respiratory arrest	1 (0.95%)	0 (0.00%)	0 (0.00%)
Sleep apnoea syndrome	0 (0.00%)	1 (0.65%)	0 (0.00%)
Vascular disorders			
Haematoma	0 (0.00%)	1 (0.65%)	0 (0.00%)
Peripheral arterial occlusive disease	1 (0.95%)	0 (0.00%)	0 (0.00%)
Thrombophlebitis superficial	1 (0.95%)	0 (0.00%)	0 (0.00%)

Other Adverse Events by System Organ Class

Time Frame	Adverse Events and Serious Adverse Events were collected for the maximum actual duration of treatment exposure and follow up for a participant per the protocol for approximately up to 5.5 years
Source Vocabulary for Table Default	MedDRA (21.0)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	5%

	Any secukinumab 75 mg N = 105	Any secukinumab 150 mg N = 155	Placebo N = 74
Arm/Group Description	Includes patients originally randomized to secukinumab 75 mg at baseline and placebo patients who were re-randomized to secukinumab 75 mg at week 16 (AEs occurring after re-randomization).	Includes patients originally randomized to secukinumab 150 mg at baseline, placebo patients re-randomized to secukinumab 150 mg at Week 16 (AEs occuring after re-randomization) and patients who up-titrated from secukinumab 75 mg to 150 mg (AEs occurring after up-titration).	Includes patients originally randomized to Placebo for AEs until the time of re-randomization (Week 16) to Secukinumab
Total participants affected	76 (72.38%)	99 (63.87%)	26 (35.14%)
Gastrointestinal disorders			
Diarrhoea	9 (8.57%)	17 (10.97%)	1 (1.35%)
General disorders and administration site conditions			

Fatigue	4 (3.81%)	5 (3.23%)	5 (6.76%)
Infections and infestations			
Bronchitis	15 (14.29%)	14 (9.03%)	1 (1.35%)
Gastroenteritis	6 (5.71%)	13 (8.39%)	1 (1.35%)
Influenza	13 (12.38%)	14 (9.03%)	0 (0.00%)
Nasopharyngitis	30 (28.57%)	35 (22.58%)	3 (4.05%)
Oral herpes	6 (5.71%)	8 (5.16%)	0 (0.00%)
Pharyngitis	6 (5.71%)	3 (1.94%)	0 (0.00%)
Rhinitis	6 (5.71%)	5 (3.23%)	1 (1.35%)
Sinusitis	5 (4.76%)	8 (5.16%)	1 (1.35%)
Upper respiratory tract infection	13 (12.38%)	16 (10.32%)	2 (2.70%)
Urinary tract infection	5 (4.76%)	9 (5.81%)	2 (2.70%)
Metabolism and nutrition disorders			
Hyperlipidaemia	5 (4.76%)	8 (5.16%)	1 (1.35%)
Musculoskeletal and connective tissue disorders			
Ankylosing spondylitis	6 (5.71%)	6 (3.87%)	1 (1.35%)
Arthralgia	8 (7.62%)	10 (6.45%)	2 (2.70%)
Back pain	7 (6.67%)	13 (8.39%)	2 (2.70%)
Bursitis	6 (5.71%)	4 (2.58%)	0 (0.00%)
Musculoskeletal pain	7 (6.67%)	8 (5.16%)	0 (0.00%)
Osteoarthritis	6 (5.71%)	4 (2.58%)	1 (1.35%)
Pain in extremity	2 (1.90%)	11 (7.10%)	1 (1.35%)

Nervous system disorders			
Dizziness	2 (1.90%)	3 (1.94%)	4 (5.41%)
Headache	9 (8.57%)	15 (9.68%)	6 (8.11%)
Respiratory, thoracic and mediastinal disorders			
Cough	5 (4.76%)	11 (7.10%)	1 (1.35%)
Oropharyngeal pain	4 (3.81%)	8 (5.16%)	2 (2.70%)
Skin and subcutaneous tissue disorders			
Rash	6 (5.71%)	4 (2.58%)	1 (1.35%)
Vascular disorders			
Hypertension	9 (8.57%)	15 (9.68%)	0 (0.00%)

Other Relevant Findings

Conclusion:

Secukinumab 150 mg sc demonstrated a rapid onset of response and superior efficacy over placebo in the treatment of patients with moderate to severe active AS as assessed by measures of clinical response, physical function, quality of life and markers of inflammation. The secukinumab 150 mg sc dose, with a subcutaneous loading and maintenance regimen gave significantly greater responses than placebo at Week 16, with respect to the primary endpoint (ASAS 20) and all secondary endpoints (ASAS 40, hsCRP, ASAS 5/6, BASDAI, SF-36 PCS and ASQoL) except for ASAS partial remission.
The safety profile of secukinumab at both doses showed no clinically meaningful differences between treatments through entire study. Overall, the present study confirmed the safety profile from the large secukinumab safety database across multiple indications with no new or unexpected safety findings.

Date of Clinical Trial Report

12-Apr-2019