NOVARTIS

Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

secukinumab

Trial Indication(s)

plaque psoriasis

Protocol Number

CAIN457ADE02

Protocol Title

A randomized, double-blind, placebo-controlled, multicenter, exploratory evaluation of surrogate markers of cardiovascular risk in patients with active chronic plaque-type psoriasis treated for up to 52 weeks with subcutaneous (s.c.) secukinumab (300 mg or 150 mg).

Clinical Trial Phase

Phase 3

Phase of Drug Development

Phase IIIb

Study Start/End Dates

Study Start Date: 1 April 2014 (Actual)
Primary Completion Date: 21 April 2016 (Actual)
Study Completion Date: 21 April 2016 (Actual)

Reason for Termination (If applicable)

Study Design/Methodology

This was an exploratory, multicenter, double-blind, randomized, placebo-controlled, parallel-group study in patients with plaque-type psoriasis, using placebo control and 2 dose sizes of secukinumab (treatment group A and B: secukinumab 300 mg or 150 mg, respectively, until W48; treatment group C and D: Placebo until W12, followed by secukinumab 300 mg or 150 mg, respectively, until W48).

Centers

Germany(50)

Objectives:

The primary objective of this study was to compare flow mediated dilation (FMD) – a measure of endothelial function – at week 12 in patients receiving 300 mg secukinumab and in patients receiving placebo.

The secondary objective of the study was to evaluate the following cardiovascular markers at weeks 4, 12, 24 and 52 (W4, W12, W24, W52): FMD (endothelial function), arterial stiffness, soluble biomarkers in the blood, total plaque burden in the carotid artery and the aorta (sub-study) measured from assessment of the vessel wall area, and composition of plaque, when present, in the carotid artery (sub-study).

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

Secukinumab 300 mg or 150 mg every 4 weeks; subcutaneous injection; batch nos.: S0004, S0005, S0006, S0008, S0009, S0014A, S0015.

Statistical Methods

Continuous outcomes were compared between treatment groups using an analysis of covariance (ANCOVA) model with factor treatment and covariate baseline value. For the primary efficacy outcome FMD at week 12, additionally a repeated measures model was calculated.

For cardiovascular markers, the mean changes from baseline were calculated together with a descriptive p-value and a 95% confidence interval (paired t-test). For measurement times up to W12, the two placebo arms were pooled. Measurements after W12 were evaluated in four groups. Odds ratios (OR) for PASI responses were calculated based on logistic regression models with factor treatment.

Study Population: Key Inclusion/Exclusion Criteria

Key Inclusion Criteria:

- Chronic moderate to severe plaque type psoriasis for at least 6 months prior to randomization with a Psoriasis Area and Severity Index (PASI) score ≥ 10 at randomization.
- Inadequate response, intolerance or contraindication to cyclosporine, methotrexate and psoralen plus ultraviolet A light treatment (PUVA) as documented in the patient's medical history or reported by the patient or determined by the investigator at screening.
- Relative contraindications such as interference of patient's lifestyle with the treatment are accepted.

Key Exclusion Criteria:

- Forms of psoriasis other than chronic plaque-type (e.g., pustular, erythrodermic and guttata psoriasis) at screening or randomization.
- Ongoing use of prohibited psoriasis and non-psoriasis treatments. Washout periods have to be adhered to.

Participant Flow Table

Overall Study

	Secukinumab 300 mg	Secukinumab 150 mg	Placebo followed by 300 mg secukinumab	Placebo followed by 150 mg secukinumab
Started	48	54	26	23
Completed	47	49	24	20
Not Completed	1	5	2	3

Adverse Event	0	2	2	2
Progressive disease	0	1	0	0
Subject/guardian decision				
Patient/guardian decision	1	2	0	1

Baseline Characteristics

	Secukinumab 300 mg	Secukinumab 150 mg	Placebo followed by 300 mg secukinumab	Placebo followed by 150 mg secukinumab	Total
Number of Participants [units: participants]	48	54	26	23	151
Gender, Male/Female (units: Participants)					
Female	11	23	8	7	49
Male	37	31	18	16	102
Age Categorical (units: Participants)					
<=18 years	0	0	0	0	0
Between 18 and 65 years	46	46	26	22	140
>=65 years	2	8	0	1	11
Age Continuous (units: years) Mean ± Standard Deviation	44.2±12.9	46.0±14.4	43.7±11.4	46.8±13.1	45.2±13.2

Region of Enrollment (units: participants)	48	54	26	23	151

Summary of Efficacy

Primary Outcome Result(s)

Flow Mediated Dilation (FMD) at Week 12 followed by secukinumab 300 mg vs pooled placebo treatment

	Secukinumab 300 mg	Placebo (Pooled)
Number of Participants Analyzed [units: participants]	39	38
Flow Mediated Dilation (FMD) at Week 12 followed by secukinumab 300 mg vs pooled placebo treatment (units: Percentage maximal increase in diameter) Mean ± Standard Deviation	5.23 ± 5.30	3.65 ± 4.07

Statistical Analysis

Groups	Secukinumab 300 mg, Placebo (Pooled)
Non-Inferiority/Equivalence Test	No
P Value	0.2230

Method	ANCOVA
Other Least Square (LS) mean difference	1.17
95 % Confidence Interval 2-Sided	-0.72 to 3.06

Secondary Outcome Result(s)

Change from baseline in Flow Mediated Dilation (FMD) at Week 4, 12, 24 and 52

	Secukinumab 300 mg	Secukinumab 150 mg	Placebo followed by 300 mg secukinumab	Placebo followed by 150 mg secukinumab
Number of Participants Analyzed [units: participants]	48	54	26	23
Change from baseline in Flow Mediated Dilation (FMD) at Week 4, 12, 24 and 52 (units: Percentage change in FMD) Mean (95% Confidence Interval)				
Week 4 (n = 37,47,21,16)	-0.7 (-1.9 to 0.5)	-0.9 (-2.4 to 0.7)	0.7 (-1.0 to 2.5)	1.4 (-0.8 to 3.6)
Week 12 (n = 39,48,21,17)	0.5 (-1.1 to 2.1)	0.1 (-1.2 to 1.5)	-0.1 (-2.7 to 2.4)	0.1 (-2.1 to 2.3)
Week 24 (n = 35,39,19,16)	-0.8 (-1.9 to 0.3)	1.0 (-0.4 to 2.4)	-0.0 (-2.6 to 2.6)	0.9 (-1.0 to 2.9)
Week 52 (n = 38,43,20,17)	2.1	2.1	2.2	1.2

	(0.8 to 3.3)	(0.7 to 3.4)	(-0.5 to 4.9)	(-1.0 to 3.5)

Change from baseline in Aortic Augmentation Index at heart rate of 75 (AIx-75) at Week 4, 12, 24 and 52

	Secukinumab 300 mg	Secukinumab 150 mg	Placebo followed by 300 mg secukinumab	Placebo followed by 150 mg secukinumab
Number of Participants Analyzed [units: participants]	48	54	26	23
Change from baseline in Aortic Augmentation Index at heart rate of 75 (AIx-75) at Week 4, 12, 24 and 52 (units: Percentage change in AIx-75) Mean (95% Confidence Interval)				
Week 4 (n = 47,52,25,21)	0.0 (-2.8 to 2.9)	0.3 (-2.0 to 2.7)	1.1 (-1.7 to 3.8)	-0.1 (-3.0 to 2.9)
Week 12 (n = 48,52,26,21)	-0.5 (-3.0 to 2.1)	1.0 (-1.7 to 3.8)	-1.1 (-5.4 to 3.3)	-0.1 (-3.4 to 3.2)
Week 24 (n = 47,50,24,21)	3.0 (0.3 to 5.6)	1.8 (-0.6 to 4.3)	1.3 (-2.7 to 5.3)	0.7 (-2.7 to 4.1)
Week 52 (n = 47,49,25,20)	1.3 (-1.5 to 4.2)	-0.1 (-2.8 to 2.7)	-1.4 (-5.8 to 2.9)	-0.9 (-4.2 to 2.5)

Change from Baseline in Pulse Wave Velocity (PWV) at Week 4, 12, 24 and 52

	Secukinumab 300 mg	Secukinumab 150 mg	Placebo Followed by 300 mg Secukinumab	Placebo Followed by 150 mg Secukinumab
Number of Participants Analyzed [units: participants]	48	54	26	23
Change from Baseline in Pulse Wave Velocity (PWV) at Week 4, 12, 24 and 52 (units: meters per second (m/s)) Mean (95% Confidence Interval)				

Week 4 (n = 192, 262, 133, 104)	0.0 (-0.2 to 0.2)	-0.2 (-0.3 to 0.0)	0 (-0.1 to 0.2)	-0.2 (-0.5 to 0.2)
Week 12 (n = 214, 255, 116, 133)	0.4 (0.2 to 0.6)	0.1 (-0.1 to 0.2)	0.1 (-0.2 to 0.4)	0.4 (0.1 to 0.7)
Week 24 (n = 205, 255, 100, 100)	0.2 (-0.1 to 0.5)	0.0 (-0.2 to 0.1)	0.2 (0.1 to 0.4)	-0.1 (-0.5 to 0.2)
Week 52 (n = 191, 228, 115, 101)	-0.1 (-0.3 to 0.0)	0.2 (-0.1 to 0.5)	0.1 (-0.2 to 0.4)	-0.2 (-0.6 to 0.2)

Change from baseline in Average wall area assessed as a measure of total plaque burden at Week 12

	Secukinumab 300 mg	Secukinumab 150 mg	Placebo followed by 300 mg secukinumab	Placebo followed by 150 mg secukinumab
Number of Participants Analyzed [units: participants]	48	54	26	23
Change from baseline in Average wall area assessed as a measure of total plaque burden at Week 12 (units: millimeter square (mm^2)) Mean (95% Confidence Interval)				
Ascending thoracic aorta (n = 10,11,4,6)	15.35 (-8.23 to 38.92)	5.91 (-13.09 to 24.91)	9.92 (-58.24 to 78.08)	6.45 (-9.26 to 22.15)
Descending thoracic aorta (n = 10,11,4,7)	2.69 (-14.18 to 19.56)	-2.94 (-13.44 to 7.57)	-4.04 (-29.61 to 21.53)	3.16 (-13.73 to 20.05)
Carotid bifurcation left (n = 11,11,4,7)	0.52 (-2.72 to 3.77)	-1.08 (-3.85 to 1.69)	3.63 (-7.82 to 15.08)	1.12 (-2.04 to 4.28)
Carotid bifurcation right (n = 11,11,4,7)	-0.77 (-3.60 to 2.06)	1.75 (-0.71 to 4.21)	-1.26 (-7.64 to 5.12)	-1.07 (-4.24 to 2.10)
Common carotid left (n = 11,11,4,6)	0.17 (-1.64 to 1.99)	1.12 (-1.80 to 4.03)	0.69 (-5.21 to 6.59)	0.12 (-1.91 to 2.15)

Common carotid right (n = 11,11,4,7)	-0.12 (-2.17 to 1.92)	0.30 (-2.76 to 3.36)	-0.38 (-6.56 to 5.80)	-0.14 (-1.60 to 1.32)
Internal carotid left (n = 9,10,4,5)	3.79 (-0.19 to 7.78)	2.09 (-0.57 to 4.75)	2.59 (-0.58 to 5.77)	-1.74 (-4.55 to 1.08)
Internal carotid right (n = 11,11,4,7)	-0.69 (-1.90 to 0.51)	0.17 (-1.96 to 2.30)	0.68 (-3.97 to 5.33)	-1.37 (-4.37 to 1.62)
Descending abdominal aorta (n = 8,9,4,6)	8.71 (-6.33 to 23.76)	-3.79 (-21.90 to 14.32)	4.56 (-52.64 to 61.77)	-0.58 (-15.51 to 14.35)

Change from baseline in Average wall area assessed as a measure of total plaque burden at Week 52

	Secukinumab 300 mg	Secukinumab 150 mg	Placebo followed by 300 mg secukinumab	Placebo followed by 150 mg secukinumab
Number of Participants Analyzed [units: participants]	48	54	26	23
Change from baseline in Average wall area assessed as a measure of total plaque burden at Week 52 (units: mm^2) Mean (95% Confidence Interval)				
Ascending thoracic aorta (n = 10,11,4,6)	14.42 (-14.93 to 43.76)	3.19 (-17.17 to 23.55)	-15.11 (-28.15 to -2.06)	9.54 (-14.71 to 33.79)
Descending thoracic aorta (n = 10,11,4,7)	3.97 (-13.42 to 21.37)	2.55 (-12.23 to 17.33)	-10.14 (-34.05 to 13.77)	1.14 (-26.76 to 29.05)
Carotid bifurcation left (n = 11,11,4,7)	2.45 (-1.55 to 6.45)	0.64 (-3.59 to 4.88)	0.58 (-9.03 to 10.20)	2.60 (-2.16 to 7.36)
Carotid bifurcation right (n = 11,11,4,7)	-1.64 (-6.02 to 2.74)	-0.05 (-3.62 to 3.51)	-3.23 (-9.86 to 3.40)	1.25 (-3.92 to 6.41)
Common carotid left (n =	1.42	1.21	0.65	1.00

11,11,4,6)	(-0.36 to 3.19)	(-1.51 to 3.93)	(-2.82 to 4.13)	(-0.83 to 2.82)
Common carotid right (n = 11,11,4,7)	0.02 (-2.54 to 2.58)	0.23 (-2.29 to 2.75)	-0.80 (-6.25 to 4.64)	-1.38 (-3.33 to 0.57)
Internal carotid left (n = 9,10,4,5)	5.43 (1.21 to 9.65)	3.59 (0.59 to 6.60)	1.06 (-2.66 to 4.78)	0.33 (-5.07 to 5.73)
Internal carotid right (n = 11,11,4,7)	-1.07 (-2.12 to -0.03)	0.71 (-1.78 to 3.21)	-0.20 (-3.89 to 3.49)	0.13 (-2.22 to 2.48)
Descending abdominal aorta (n = 8,9,4,6)	10.56 (-8.37 to 29.48)	-4.36 (-17.90 to 9.19)	12.46 (-46.12 to 71.05)	11.82 (-15.26 to 38.90)

Change from Baseline in High sensitivity C-reactive protein (hsCRP) at Week 4, 12, 24 and 52

	Secukinumab 300 mg	Secukinumab 150 mg	Placebo followed by 300 mg secukinumab	Placebo followed by 150 mg secukinumab
Number of Participants Analyzed [units: participants]	48	54	26	23
Change from Baseline in High sensitivity C-reactive protein (hsCRP) at Week 4, 12, 24 and 52 (units: Milligrams per deciliter (mg/dL)) Mean (95% Confidence Interval)				
Week 4 (n = 48,53,26,21)	0.0 (-0.2 to 0.2)	-0.2 (-0.4 to -0.1)	-0.0 (-0.2 to 0.2)	0.1 (-0.1 to 0.3)
Week 12 (n = 48,54,26,21)	-0.0 (-0.3 to 0.3)	-0.2 (-0.3 to 0.0)	-0.3 (-0.8 to 0.1)	0.1 (-0.4 to 0.6)
Week 24 (n = 48,52,25,21)	-0.0 (-0.3 to 0.2)	-0.0 (-0.3 to 0.2)	0.1 (-0.2 to 0.4)	-0.4 (-0.9 to 0.1)
Week 52 (n = 48,50,26,20)	-0.1 (-0.3 to 0.1)	-0.2 (-0.4 to -0.0)	-0.3 (-0.8 to 0.2)	-0.5 (-1.1 to 0.0)

Change from Baseline in S-100 protein B (total) at Week 4, 12, 24 and 52

	Secukinumab 300 mg	Secukinumab 150 mg	Placebo followed by 300 mg secukinumab	Placebo followed by 150 mg secukinumab
Number of Participants Analyzed [units: participants]	48	54	26	23
Change from Baseline in S-100 protein B (total) at Week 4, 12, 24 and 52 (units: Microgram per Liter (ug/L)) Mean (95% Confidence Interval)				
Week 4 (n = 48,53,26,22)	-0.0 (-0.0 to -0.0)	-0.0 (-0.0 to 0.0)	0.0 (-0.0 to 0.0)	0.0 (-0.0 to 0.0)
Week 12 (n = 48,52,26,22)	-0.0 (-0.0 to 0.0)	-0.0 (-0.0 to 0.0)	0.0 (-0.0 to 0.0)	0.0 (0.0 to 0.0)
Week 24 (n = 48,51,25,22)	-0.0 (-0.0 to 0.0)	0.0 (-0.0 to 0.0)	0.0 (-0.0 to 0.0)	0.0 (-0.0 to 0.0)
Week 52 (n = 48,51,26,22)	-0.0 (-0.0 to 0.0)	-0.0 (-0.0 to -0.0)	0.0 (-0.0 to 0.0)	-0.0 (-0.0 to 0.0)

Change from Baseline in Chemokine (c-c motif) ligand 5 (CCL5), Monocyte chemoattractant protein 1 (MCP-1) and Macrophage inflammatory proteins (MIP) 1 alpha and 1 beta at Week 4, 12, 24 and 52

	Secukinumab 300 mg	Secukinumab 150 mg	Placebo followed by 300 mg secukinumab	Placebo followed by 150 mg secukinumab
Number of Participants Analyzed [units: participants]	48	54	26	23
Change from Baseline in Chemokine (c-c motif) ligand 5 (CCL5), Monocyte chemoattractant protein 1 (MCP-1) and Macrophage inflammatory proteins (MIP) 1 alpha and 1 beta at Week 4, 12, 24 and 52 (units: picograms per milliliter (pg/mL)) Mean (95% Confidence Interval)				

CCL5 Week 4 (n = 48,54,26,22)	-1000 (-3106 to 1094)	1649 (-597 to 3895)	27.0 (-3943 to 3997)	-2000 (-5056 to 281.3)
CCL5 Week 12 (n = 48,54,26,22)	2116 (-2368 to 6599)	5185 (840.3 to 9530)	4393 (-1598 to 10383)	3002 (-1806 to 7809)
CCL5 Week 24 (n = 48,52,25,22)	7772 (3766 to 11777)	10000 (6437 to 14394)	11000 (2117 to 20176)	9168 (2124 to 16212)
CCL5 Week 52 (n = 48,51,25,22)	1515 (-2478 to 5507)	3577 (-737 to 7891)	-597 (-3340 to 2145)	2308 (-2558 to 7175)
MCP-1 Week 4 (n = 48,54,26,22)	-7.0 (-21.8 to 7.7)	1.4 (-17.4 to 20.2)	-25 (-57.2 to 8.0)	17.5 (-43.1 to 78.0)
MCP-1 Week 12 (n = 48,54,26,22)	18.4 (-1.9 to 38.7)	28.6 (-8.4 to 65.7)	11.3 (-40.9 to 63.5)	21.5 (-18.3 to 61.2)
MCP-1 Week 24 (n = 48,52,25,22)	39.8 (-0.6 to 80.3)	241 (-203 to 685.7)	-20 (-53.9 to 14.2)	33.4 (8.3 to 58.5)
MCP-1 Week 52 (n = 48,51,25,22)	22.1 (-18.1 to 62.4)	25.4 (-21.7 to 72.6)	-11 (-60.6 to 38.6)	109 (-13.3 to 230.9)
MIP-1A Week 4 (n = 48,54,26,22)	-0.1 (-2.1 to 1.9)	0.1 (-1.6 to 1.8)	0.5 (-2.5 to 3.5)	-0.6 (-2.3 to 1.2)
MIP-1A Week 12 (n = 48,54,26,22)	0.2 (-2.8 to 3.3)	2.2 (-1.0 to 5.3)	-3.6 (-7.0 to -0.3)	0.9 (-3.0 to 4.8)
MIP-1A Week 24 (n = 48,52,22,22)	-0.2 (-2.9 to 2.4)	-0.5 (-3.6 to 2.6)	-4.7 (-8.4 to -1.0)	1.7 (-1.3 to 4.7)
MIP-1A Week 52 (n = 48,51,25,22)	4.3 (-0.1 to 8.7)	0.8 (-3.0 to 4.5)	1.7 (-6.0 to 9.5)	20.1 (4.7 to 35.6)
MIP-1B Week 4 (n = 48,54,26,22)	-24 (-50.8 to 3.0)	-2.6 (-24.8 to 19.5)	-16 (-57.5 to 25.8)	-20 (-54.4 to 15.3)
MIP-1B Week 12 (n = 48,54,26,22)	-49 (-80.9 to -	-34 (-69.0 to 1.4)	-65 (-106 to -24.7)	-68 (-116 to -20.5)

	16.6)			
MIP-1B Week 24 (n = 48,52,25,22)	-52 (-130 to 26.7)	-97 (-133 to -61.3)	-161 (-207 to -114)	79.4 (-261 to 420.3)
MIP-1B Week 52 (n = 48,51,25,22)	-41 (-73.6 to -8.6)	-59 (-89.0 to -29.7)	-73 (-122 to -24.2)	-31 (-109 to 46.8)

Change from Baseline in Fasting plasma glucose (FPG) at Week 4, 12, 24 and 52

	Secukinumab 300 mg	Secukinumab 150 mg	Placebo followed by 300 mg secukinumab	Placebo followed by 150 mg secukinumab
Number of Participants Analyzed [units: participants]	48	54	26	23
Change from Baseline in Fasting plasma glucose (FPG) at Week 4, 12, 24 and 52 (units: mg/dL) Mean (95% Confidence Interval)				
Week 4 (n = 47,53,26,22)	1.5 (-1.0 to 4.0)	-1.6 (-4.6 to 1.3)	0.9 (-4.4 to 6.1)	0.2 (-5.2 to 5.6)
Week 12 (n = 47,53,26,22)	3.5 (-0.0 to 7.0)	1.1 (-4.0 to 6.2)	5.3 (-2.2 to 12.8)	-1.5 (-7.1 to 4.0)
Week 24 (n = 47,51,25,22)	2.5 (0.0 to 5.0)	1.4 (-6.3 to 9.1)	12.1 (-10.8 to 35.0)	-1.4 (-7.7 to 5.0)
Week 52 (n = 46,51,26,22)	-0.8 (-3.5 to 2.0)	0.7 (-3.0 to 4.4)	8.7 (-7.5 to 25.0)	0.9 (-6.7 to 8.6)

Change from Baseline in Fasting Insulin at Week 4, 12, 24 and 52

	Secukinumab 300 mg	Secukinumab 150 mg	Placebo followed by 300 mg secukinumab	Placebo followed by 150 mg secukinumab

Number of Participants Analyzed [units: participants]	48	54	26	23
Change from Baseline in Fasting Insulin at Week 4, 12, 24 and 52 (units: micro units per millilitre (uU/mL)) Mean (95% Confidence Interval)				
Week 4 (n = 48,53,26,22)	0.4 (-2.0 to 2.7)	0.4 (-2.3 to 3.0)	-4.7 (-17.4 to 8.1)	-0.5 (-4.8 to 3.7)
Week 12 (n = 48,52,26,22)	-1.4 (-5.1 to 2.4)	1.1 (-2.7 to 4.8)	-2.2 (-9.2 to 4.7)	-0.1 (-4.9 to 4.7)
Week 24 (n = 48,51,25,22)	-1.0 (-4.1 to 2.0)	0.5 (-3.7 to 4.8)	-5.3 (-18.5 to 8.0)	-2.0 (-6.1 to 2.0)
Week 52 (n = 48,51,26,22)	-0.4 (-4.3 to 3.6)	1.5 (-1.3 to 4.2)	-1.2 (-7.5 to 5.1)	3.0 (-5.2 to 11.3)

Change from Baseline in Homeostatic Model Assessment (HOMA) beta-cell function at Week 4, 12, 24 and 52

	Secukinumab 300 mg	**Secukinumab 150 mg**	**Placebo followed by 300 mg secukinumab**	**Placebo followed by 150 mg secukinumab**
Number of Participants Analyzed [units: participants]	48	54	26	23
Change from Baseline in Homeostatic Model Assessment (HOMA) beta-cell function at Week 4, 12, 24 and 52 (units: Percentage) Mean (95% Confidence Interval)				
Week 4 (n = 42,51,24,21)	-18 (-64.7 to 28.2)	-0.2 (-25.7 to 25.3)	-28 (-88.4 to 33.0)	-8.9 (-38.5 to 20.7)
Week 12 (n = 44,50,23,22)	-16 (-74.4 to 41.5)	3.9 (-32.0 to 39.8)	-29 (-100 to 41.6)	16.6 (-20.6 to 53.8)
Week 24 (n = 44,50,24,22)	-25 (-53.9 to 3.5)	-8.2 (-40.2 to 23.9)	-35 (-111 to 40.7)	-26 (-63.2 to 12.0)

Week 52 (n = 43,50,25,22)	11.5 (-40.5 to 63.5)	-1.6 (-32.6 to 29.4)	9.3 (-56.4 to 75.1)	11.6 (-26.6 to 49.7)

Change from Baseline in Homeostatic Model Assessment (HOMA) insulin resistance at Week 4, 12, 24 and 52

	Secukinumab 300 mg	Secukinumab 150 mg	Placebo followed by 300 mg secukinumab	Placebo followed by 150 mg secukinumab
Number of Participants Analyzed [units: participants]	48	54	26	23
Change from Baseline in Homeostatic Model Assessment (HOMA) insulin resistance at Week 4, 12, 24 and 52 (units: Insulin Resistance Index) Mean (95% Confidence Interval)				
Week 4 (n = 42,51,24,21)	0.3 (-0.6 to 1.2)	0.1 (-0.9 to 1.0)	-1.1 (-5.2 to 3.1)	-0.3 (-2.0 to 1.3)
Week 12 (n = 44,50,23,22)	-0.1 (-1.5 to 1.4)	0.6 (-0.7 to 1.8)	-0.1 (-2.5 to 2.3)	-0.4 (-2.0 to 1.3)
Week 24 (n = 44,50,24,22)	-0.3 (-1.1 to 0.6)	0.6 (-1.3 to 2.5)	-1.1 (-5.0 to 2.8)	-0.7 (-2.2 to 0.8)
Week 52 (n = 43,50,25,22)	-0.2 (-1.2 to 0.9)	0.6 (-0.3 to 1.4)	-0.2 (-2.8 to 2.4)	0.7 (-1.9 to 3.4)

Change from Baseline in Hemoglobin A1c (glycated hemoglobin) at Week 4, 12, 24 and 52

	Secukinumab 300 mg	Secukinumab 150 mg	Placebo followed by 300 mg secukinumab	Placebo followed by 150 mg secukinumab
Number of Participants Analyzed [units: participants]	48	54	26	23
Change from Baseline in Hemoglobin A1c (glycated hemoglobin) at Week 4, 12, 24 and 52 (units: millimole per mole of Haemoglobin)				

Mean (95% Confidence Interval)				
Week 4 (n = 48,52,26,22)	0.2 (-0.5 to 0.8)	-0.4 (-1.0 to 0.3)	-0.7 (-2.3 to 1.0)	-0.4 (-1.2 to 0.4)
Week 12 (n = 48,54,26,22)	0.4 (-0.7 to 1.5)	-0.4 (-2.2 to 1.4)	-1.2 (-3.8 to 1.3)	0.1 (-0.8 to 1.0)
Week 24 (n = 48,52,25,22)	-0.4 (-1.7 to 1.0)	-1.2 (-2.9 to 0.5)	-0.1 (-2.4 to 2.1)	-1.2 (-2.9 to 0.6)
Week 52 (n = 48,52,26,22)	-1.1 (-2.3 to 0.1)	-2.8 (-6.1 to 0.4)	-1.9 (-4.3 to 0.6)	-2.1 (-3.0 to 1.2)

Change from Baseline in Sex hormone-binding globulin (SHBG) at Week 4, 12, 24 and 52

	Secukinumab 300 mg	Secukinumab 150 mg	Placebo followed by 300 mg secukinumab	Placebo followed by 150 mg secukinumab
Number of Participants Analyzed [units: participants]	48	54	26	23
Change from Baseline in Sex hormone-binding globulin (SHBG) at Week 4, 12, 24 and 52 (units: nanomole per Liter (nmol/L)) Mean (95% Confidence Interval)				
Week 4 (n = 48,53,26,21)	0.1 (-1.8 to 2.1)	3.7 (-3.0 to 10.4)	4.7 (-4.2 to 13.5)	-0.3 (-4.0 to 3.5)
Week 12 (n = 48,54,26,21)	-0.1 (-3.4 to 3.2)	1.1 (-1.8 to 4.1)	3.7 (-1.6 to 9.1)	4.1 (-0.2 to 8.4)
Week 24 (n = 48,52,25,21)	-1.5 (-5.1 to 2.2)	3.2 (-0.9 to 7.2)	1.7 (-2.9 to 6.3)	2.6 (-1.5 to 6.7)
Week 52 (n = 48,50,26,20)	-3.1 (-10.8 to 4.6)	5.9 (-1.3 to 13.0)	-2.6 (-14.9 to 9.6)	3.2 (-4.3 to 10.8)

Change from Baseline in Triglycerides, Total cholesterol, Low density lipoprotein (LDL), High density lipoprotein (HDL), Apolipoprotein A-1 (ApoA-1) and Apolipoprotein B (ApoB) at Week 4, 12, 24 and 52

	Secukinumab 300 mg	Secukinumab 150 mg	Placebo followed by 300 mg secukinumab	Placebo followed by 150 mg secukinumab
Number of Participants Analyzed [units: participants]	48	54	26	23
Change from Baseline in Triglycerides, Total cholesterol, Low density lipoprotein (LDL), High density lipoprotein (HDL), Apolipoprotein A-1 (ApoA-1) and Apolipoprotein B (ApoB) at Week 4, 12, 24 and 52 (units: mg/dL) Mean (95% Confidence Interval)				
Triglycerides Week 4 (n = 48,53,26,21)	-1.8 (-15.5 to 12.0)	6.5 (-5.9 to 18.9)	12.7 (-12.2 to 37.7)	27.5 (-6.6 to 61.6)
Triglycerides Week 12 (n = 48,54,26,21)	-9.3 (-20.8 to 2.3)	4.0 (-9.3 to 17.3)	5.9 (-32.4 to 44.2)	2.7 (-18.3 to 23.8)
Triglycerides Week 24 (n = 48,52,25,21)	4.6 (-16.6 to 25.8)	3.9 (-9.1 to 16.9)	32.8 (-19.7 to 85.2)	17.1 (-2.3 to 36.5)
Triglycerides Week 52 (n = 48,50,26,20)	64.6 (-44.0 to 173.2)	2.6 (-11.7 to 16.9)	-6.0 (-54.3 to 42.3)	11.9 (-8.6 to 32.3)
Total cholesterol Week 4 (n = 48,53,26,21)	0.4 (-6.4 to 7.1)	7.1 (1.1 to 13.2)	4.8 (-3.2 to 12.8)	-2.7 (-10.0 to 4.7)
Total cholesterol Week 12 (n = 48,54,26,21)	3.1 (-3.1 to 9.4)	3.6 (-4.1 to 11.2)	10.0 (2.8 to 17.1)	-4.2 (-11.2 to 2.8)
Total cholesterol Week 24 (n = 48,52,25,21)	0.9 (-5.2 to 7.1)	0.6 (-4.9 to 6.1)	7.2 (-1.5 to 16.0)	-3.2 (-12.0 to 5.5)
Total cholesterol Week 52 (n = 48,50,26,20)	7.8 (0.0 to 15.6)	2.3 (-5.2 to 9.9)	8.9 (2.1 to 15.7)	2.9 (-5.9 to 11.7)
LDL Week 4 (n = 48,53,26,21)	1.1 (-4.6 to 6.8)	6.8 (0.8 to 12.8)	5.2 (-2.0 to 12.4)	-5.6 (-12.1 to 0.8)
LDL Week 12 (n = 48,54,26,21)	2.9 (-2.2 to 7.9)	2.7 (-4.8 to 10.1)	9.5 (3.4 to 15.5)	-5.6 (-12.7 to 1.5)
LDL Week 24 (n =	-2.7	-1.3	1.1	-11

48,52,25,21)	(-8.1 to 2.7)	(-6.9 to 4.4)	(-7.4 to 9.5)	(-18.9 to -2.4)
LDL Week 52 (n = 48,50,26,20)	1.7 (-6.5 to 9.9)	-0.9 (-8.4 to 6.5)	8.2 (1.3 to 15.0)	1.1 (-8.4 to 10.5)
HDL Week 4 (n = 48,53,26,21)	-0.6 (-2.6 to 1.3)	0.4 (-1.5 to 2.2)	0.3 (-2.3 to 2.9)	-1.3 (-4.6 to 2.0)
HDL Week 12 (n = 48,54,26,21)	-0.4 (-2.4 to 1.6)	0.2 (-1.8 to 2.2)	1.0 (-1.2 to 3.3)	-0.5 (-4.9 to 3.8)
HDL Week 24 (n = 48,52,25,21)	1.2 (-1.5 to 3.9)	0.3 (-2.3 to 2.8)	-1.1 (-3.4 to 1.3)	0.5 (-4.1 to 5.1)
HDL Week 52 (n = 48,50,26,20)	0.1 (-2.1 to 2.4)	1.8 (-0.5 to 4.2)	-0.3 (-2.9 to 2.4)	-1.4 (-4.6 to 1.8)
ApoA-1 Week 4 (n = 48,53,26,21)	0.3 (-5.1 to 5.7)	0.9 (-4.0 to 5.7)	7.7 (-0.6 to 15.9)	-5.5 (-12.0 to 1.0)
ApoA-1 Week 12 (n = 48,54,26,21)	4.0 (-2.0 to 10.1)	2.4 (-1.9 to 6.8)	7.1 (1.2 to 12.9)	-3.3 (-12.1 to 5.5)
ApoA-1 Week 24 (n = 48,52,25,21)	5.5 (-0.9 to 12.0)	2.8 (-3.0 to 8.6)	3.0 (-3.3 to 9.3)	-3.1 (-11.3 to 5.1)
ApoA-1 Week 52 (n = 48,50,26,20)	-4.5 (-10.0 to 0.9)	-6.0 (-11.6 to -0.3)	-5.5 (-14.9 to 3.9)	-13 (-22.3 to -3.1)
ApoB Week 4 (n = 48,53,26,21)	1.5 (-2.7 to 5.6)	3.6 (0.5 to 6.6)	2.7 (-1.1 to 6.5)	-2.5 (-7.7 to 2.8)
ApoB Week 12 (n = 48,54,26,21)	4.0 (0.6 to 7.4)	3.4 (-0.5 to 7.3)	7.4 (3.9 to 11.0)	-1.0 (-7.0 to 4.9)
ApoB Week 24 (n = 48,52,25,21)	1.0 (-2.8 to 4.8)	2.0 (-1.3 to 5.3)	5.6 (1.4 to 9.9)	-4.2 (-10.7 to 2.3)
ApoB Week 52 (n = 48,50,26,20)	3.7 (-2.2 to 9.6)	2.3 (-1.8 to 6.4)	6.7 (3.0 to 10.5)	-0.2 (-5.4 to 5.0)

Change from Baseline in Adiponectin at Week 4, 12, 24 and 52

	Secukinumab 300 mg	Secukinumab 150 mg	Placebo followed by 300 mg	Placebo followed by 150 mg

			secukinumab	secukinumab
Number of Participants Analyzed [units: participants]	48	54	26	23
Change from Baseline in Adiponectin at Week 4, 12, 24 and 52 (units: ug/mL) Mean (95% Confidence Interval)				
Week 4 (n = 48,53,26,22)	-0.5 (-1.0 to -0.1)	0.2 (-0.4 to 0.8)	-0.1 (-0.8 to 0.5)	-0.6 (-1.2 to -0.0)
Week 12 (n = 48,52,26,22)	-0.5 (-1.1 to -0.0)	-0.2 (-0.7 to 0.3)	0.5 (0.1 to 0.9)	0.3 (-0.7 to 1.3)
Week 24 (n = 48,51,25,22)	0.3 (-0.3 to 0.9)	0.1 (-0.5 to 0.7)	0.7 (-0.3 to 1.8)	-0.6 (-1.6 to 0.3)
Week 52 (n = 48,51,26,22)	-1.1 (-1.6 to -0.6)	-0.9 (-1.5 to -0.3)	-0.4 (-1.0 to 0.2)	-1.1 (-2.0 to -0.3)

Change from Baseline in Leptin at Week 4, 12, 24 and 52

	Secukinumab 300 mg	Secukinumab 150 mg	Placebo followed by 300 mg secukinumab	Placebo followed by 150 mg secukinumab
Number of Participants Analyzed [units: participants]	48	54	26	23
Change from Baseline in Leptin at Week 4, 12, 24 and 52 (units: ng/mL (nanogram per milliliter)) Mean (95% Confidence Interval)				
Week 4 (n = 48,53,26,22)	-0.6 (-1.8 to 0.7)	1.0 (-0.1 to 2.2)	-0.2 (-1.6 to 1.2)	0.3 (-1.2 to 1.9)
Week 12 (n = 48,52,26,22)	0.2 (-0.7 to 1.1)	0.1 (-0.9 to 1.2)	0.7 (-1.0 to 2.4)	-0.3 (-1.7 to 1.2)
Week 24 (n = 48,51,25,22)	0.2 (-0.7 to 1.2)	1.0 (-0.5 to 2.4)	-0.3 (-2.8 to 2.3)	-1.4 (-4.9 to 2.1)

Week 52 (n = 48,51,26,22)	0.2 (-1.0 to 1.3)	-0.5 (-1.6 to 0.7)	-0.4 (-3.8 to 3.0)	-2.9 (-5.7 to 0.0)

Summary of Safety

Safety Results

Serious Adverse Events by System Organ Class

Time Frame	From signing of Informed Consent up to 30 days post last drug treatment.
Source Vocabulary for Table Default	MedDRA (19.0)
Assessment Type for Table Default	Systematic Assessment

	Secukinumab (300 mg) up to Week 12 N = 48	Secukinumab (150 mg) up to Week 12 N = 54	Placebo up to Week 12 N = 49	Secukinumab (300 mg) after Week 12 N = 48	Secukinumab (150 mg) after Week 12 N = 54	Placebo followed by secukinumab (300 mg) after Week 12 N = 26	Placebo followed by secukinumab (150 mg) after Week 12 N = 23
Total participants affected	1 (2.08%)	0 (0.00%)	2 (4.08%)	6 (12.50%)	6 (11.11%)	0 (0.00%)	1 (4.35%)
EAR AND LABYRINTH DISORDERS							
VESTIBULAR DISORDER	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
GASTROINTESTINAL DISORDERS							
COLITIS	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)

DUODENAL ULCER	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
GASTRIC ULCER	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
GASTRITIS EROSIVE	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
INFECTIONS AND INFESTATIONS							
ANAL ABSCESS	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
ERYSIPELAS	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
HELICOBACTER INFECTION	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
PNEUMONIA BACTERIAL	1 (2.08%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS							
CLAVICLE FRACTURE	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)
JOINT DISLOCATION	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS							
BACK PAIN	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
HAEMARTHROSIS	0 (0.00%)	0 (0.00%)	1 (2.04%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
RHEUMATOID ARTHRITIS	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)
VERTEBRAL FORAMINAL STENOSIS	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)							
OVARIAN CANCER	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)

NERVOUS SYSTEM DISORDERS							
CEREBRAL INFARCTION	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)
TRANSIENT ISCHAEMIC ATTACK	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS							
UTERINE POLYP	0 (0.00%)	0 (0.00%)	1 (2.04%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS							
PSORIASIS	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)

Other Adverse Events by System Organ Class

Time Frame	From signing of Informed Consent up to 30 days post last drug treatment.
Source Vocabulary for Table Default	MedDRA (19.0)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	3%

	Secukinumab (300 mg) up to Week 12 N = 48	**Secukinumab (150 mg) up to Week 12 N = 54**	**Placebo up to Week 12 N = 49**	**Secukinumab (300 mg) after Week 12 N = 48**	**Secukinumab (150 mg) after Week 12 N = 54**	**Placebo followed by secukinumab (300 mg) after Week 12 N = 26**	**Placebo followed by secukinumab (150 mg) after Week 12 N = 23**
Total participants affected	29 (60.42%)	36 (66.67%)	35 (71.43%)	36 (75.00%)	43 (79.63%)	21 (80.77%)	19 (82.61%)

BLOOD AND LYMPHATIC SYSTEM DISORDERS							
LYMPHADENOPATHY	1 (2.08%)	2 (3.70%)	1 (2.04%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
NEUTROPENIA	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
EYE DISORDERS							
CONJUNCTIVITIS ALLERGIC	0 (0.00%)	2 (3.70%)	0 (0.00%)	1 (2.08%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
DRY EYE	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
EYE SWELLING	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
GASTROINTESTINAL DISORDERS							
ABDOMINAL PAIN UPPER	0 (0.00%)	1 (1.85%)	1 (2.04%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)
BURNING MOUTH SYNDROME	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)
CONSTIPATION	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
DIARRHOEA	2 (4.17%)	2 (3.70%)	1 (2.04%)	0 (0.00%)	3 (5.56%)	3 (11.54%)	1 (4.35%)
DYSPEPSIA	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
DYSPHAGIA	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.17%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
GASTRITIS	1 (2.08%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (3.70%)	0 (0.00%)	0 (0.00%)
GASTROOESOPHAGEAL REFLUX DISEASE	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.17%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
GLOSSITIS	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
HAEMORRHOIDS	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.17%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
NAUSEA	1 (2.08%)	2 (3.70%)	0 (0.00%)	1 (2.08%)	1 (1.85%)	1 (3.85%)	1 (4.35%)
STOMATITIS	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
TOOTHACHE	1 (2.08%)	0 (0.00%)	0 (0.00%)	2 (4.17%)	1 (1.85%)	1 (3.85%)	0 (0.00%)

GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS							
FATIGUE	0 (0.00%)	2 (3.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
INJECTION SITE PAIN	0 (0.00%)	0 (0.00%)	1 (2.04%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)
OEDEMA PERIPHERAL	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	1 (4.35%)
INFECTIONS AND INFESTATIONS							
BRONCHITIS	1 (2.08%)	1 (1.85%)	0 (0.00%)	3 (6.25%)	1 (1.85%)	0 (0.00%)	0 (0.00%)
CANDIDA INFECTION	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.17%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
CONJUNCTIVITIS	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.85%)	2 (7.69%)	0 (0.00%)
ECTHYMA	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
FUNGAL INFECTION	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
GASTROENTERITIS	2 (4.17%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (3.70%)	0 (0.00%)	0 (0.00%)
GASTROINTESTINAL CANDIDIASIS	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
GASTROINTESTINAL INFECTION	0 (0.00%)	0 (0.00%)	1 (2.04%)	2 (4.17%)	2 (3.70%)	0 (0.00%)	0 (0.00%)
GINGIVITIS	0 (0.00%)	0 (0.00%)	1 (2.04%)	1 (2.08%)	0 (0.00%)	0 (0.00%)	1 (4.35%)
HORDEOLUM	0 (0.00%)	2 (3.70%)	0 (0.00%)	1 (2.08%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
IMPETIGO	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.85%)	1 (3.85%)	0 (0.00%)
LARYNGITIS	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)
NASOPHARYNGITIS	10 (20.83%)	14 (25.93%)	18 (36.73%)	21 (43.75%)	25 (46.30%)	10 (38.46%)	10 (43.48%)
ORAL CANDIDIASIS	1 (2.08%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
ORAL HERPES	0 (0.00%)	2 (3.70%)	0 (0.00%)	2 (4.17%)	2 (3.70%)	1 (3.85%)	1 (4.35%)
OTITIS EXTERNA	1 (2.08%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
OTITIS MEDIA	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (3.70%)	0 (0.00%)	0 (0.00%)
PARONYCHIA	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)

PERIODONTITIS	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	3 (5.56%)	1 (3.85%)	0 (0.00%)
PHARYNGITIS	0 (0.00%)	2 (3.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
PULPITIS DENTAL	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)
RHINITIS	1 (2.08%)	0 (0.00%)	2 (4.08%)	2 (4.17%)	3 (5.56%)	1 (3.85%)	4 (17.39%)
ROOT CANAL INFECTION	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
SINUSITIS	2 (4.17%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	2 (3.70%)	0 (0.00%)	0 (0.00%)
SKIN CANDIDA	0 (0.00%)	2 (3.70%)	0 (0.00%)	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)
UPPER RESPIRATORY TRACT INFECTION	0 (0.00%)	2 (3.70%)	1 (2.04%)	1 (2.08%)	0 (0.00%)	0 (0.00%)	1 (4.35%)
URINARY TRACT INFECTION	0 (0.00%)	3 (5.56%)	1 (2.04%)	1 (2.08%)	1 (1.85%)	0 (0.00%)	1 (4.35%)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS							
ARTHROPOD BITE	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.17%)	1 (1.85%)	1 (3.85%)	1 (4.35%)
BURNS FIRST DEGREE	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
BURSA INJURY	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)
CONTUSION	0 (0.00%)	2 (3.70%)	1 (2.04%)	1 (2.08%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
LACERATION	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (6.25%)	0 (0.00%)	1 (3.85%)	1 (4.35%)
MUSCLE RUPTURE	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
THERMAL BURN	0 (0.00%)	1 (1.85%)	0 (0.00%)	2 (4.17%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
METABOLISM AND NUTRITION DISORDERS							
DECREASED APPETITE	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS							
ARTHRALGIA	1 (2.08%)	2 (3.70%)	5 (10.20%)	5 (10.42%)	3 (5.56%)	0 (0.00%)	3 (13.04%)

BACK PAIN	2 (4.17%)	2 (3.70%)	1 (2.04%)	4 (8.33%)	4 (7.41%)	5 (19.23%)	1 (4.35%)
MUSCLE SPASMS	1 (2.08%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
MUSCULOSKELETAL PAIN	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.17%)	1 (1.85%)	1 (3.85%)	0 (0.00%)
PAIN IN EXTREMITY	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (6.25%)	2 (3.70%)	1 (3.85%)	1 (4.35%)
SPINAL PAIN	0 (0.00%)	0 (0.00%)	1 (2.04%)	0 (0.00%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)							
PYOGENIC GRANULOMA	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)
SKIN PAPILLOMA	2 (4.17%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	0 (0.00%)	1 (3.85%)	1 (4.35%)
NERVOUS SYSTEM DISORDERS							
DIZZINESS	1 (2.08%)	1 (1.85%)	1 (2.04%)	0 (0.00%)	1 (1.85%)	1 (3.85%)	0 (0.00%)
HEADACHE	4 (8.33%)	6 (11.11%)	2 (4.08%)	7 (14.58%)	7 (12.96%)	2 (7.69%)	0 (0.00%)
PARAESTHESIA	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)
RENAL AND URINARY DISORDERS							
HAEMATURIA	2 (4.17%)	2 (3.70%)	0 (0.00%)	1 (2.08%)	0 (0.00%)	2 (7.69%)	0 (0.00%)
NEPHROLITHIASIS	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS							
DYSMENORRHOEA	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
MENOPAUSAL SYMPTOMS	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS							

COUGH	2 (4.17%)	0 (0.00%)	3 (6.12%)	2 (4.17%)	4 (7.41%)	1 (3.85%)	0 (0.00%)
NASAL INFLAMMATION	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
OROPHARYNGEAL PAIN	1 (2.08%)	0 (0.00%)	1 (2.04%)	1 (2.08%)	3 (5.56%)	1 (3.85%)	0 (0.00%)
RHINITIS ALLERGIC	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (7.69%)	0 (0.00%)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS							
ALOPECIA	0 (0.00%)	2 (3.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
DERMATITIS	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	1 (1.85%)	1 (3.85%)	0 (0.00%)
DERMATITIS ATOPIC	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
ECZEMA	1 (2.08%)	2 (3.70%)	0 (0.00%)	1 (2.08%)	1 (1.85%)	0 (0.00%)	1 (4.35%)
ERYTHEMA	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
INTERTRIGO	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.85%)	1 (3.85%)	1 (4.35%)
PAPULE	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.85%)	1 (3.85%)	0 (0.00%)
PRURITUS	2 (4.17%)	0 (0.00%)	2 (4.08%)	2 (4.17%)	2 (3.70%)	1 (3.85%)	1 (4.35%)
PSORIASIS	2 (4.17%)	0 (0.00%)	1 (2.04%)	2 (4.17%)	1 (1.85%)	0 (0.00%)	1 (4.35%)
SEBORRHOEIC DERMATITIS	0 (0.00%)	0 (0.00%)	2 (4.08%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
SKIN FISSURES	1 (2.08%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (3.85%)	0 (0.00%)
SKIN REACTION	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.35%)
VASCULAR DISORDERS							
HYPERTENSION	1 (2.08%)	1 (1.85%)	1 (2.04%)	1 (2.08%)	2 (3.70%)	1 (3.85%)	0 (0.00%)

Other Relevant Findings

Conclusion:

The results of the primary analysis show that the mean unadjusted FMD values at W12 were slightly, but not statistically significantly higher in the 300 mg group than in the (pooled) placebo group. Analysis with an ANCOVA model – to control for baseline differences in FMD – did not indicate a statistically significant difference among the groups:

Treatment / Contrast	N	Mean ± SD [%]	LS-mean [%] (95% CI) *	p value *
Secukinumab 300 mg	39	5.23 ± 5.30	5.09 (3.76; 6.41)	
Placebo	38	3.65 ± 4.07	3.92 (2.57; 5.26)	
300 mg – placebo			1.17 (-0.72; 3.06)	0.22

* Analysis of covariance with factor treatment and covariate baseline value. Please note that p-values have only descriptive function in this study.
LS-mean = least squares mean (group mean adjusted for covariate); CI = confidence interval.

Analysis with t-test indicated that FMD at W52 was significantly increased *vs* baseline, across both dose levels (2.0%; 95%CI: [1.2; 2.8]; $p < 0.01$).

The effects on other cardiovascular markers were minor and inhomogeneous.

Safety results: The safety profile obtained in this study was consistent with the profile described in the current Summary of Product Characteristics for Cosentyx 150 mg. The most frequently reported AEs were nasopharyngitis and other infections.

No new safety signals were detected. No deaths occurred during this study. Three patients experienced SAEs up to W12; 1 patient in the 300 mg group and 2 patients in the placebo group. After W12, 13 patients in total experienced SAEs, 6 each in the 300 mg and the 150 mg group and 1 patient in the placebo/150 mg group. In two cases – erysipelas in a 29-year old woman and bacterial pneumonia in a 67-year old man – the investigator considered the SAE to be related to the administration of the study medication. Study treatment (300 mg secukinumab) was continued in both patients.

The safety profile obtained in this study was consistent with the profile described in the current Summary of Product Characteristics for Cosentyx. No new safety signals were detected. The patient population in this study was relatively healthy and at a low cardiovascular risk. Also, the duration of placebo control was only 12 weeks, which makes it difficult to identify long-term effects. FMD was one of the few cardiovascular markers that showed relevant impairment at baseline. This is in line with a very early stage of developing atherosclerosis. A trend towards improvement in FMD could be observed in the 300 mg arm vs placebo at week 12, which was not statistically significant.

However, improvement continued and reached statistical significance vs. baseline at week 52. Also, there was a non-significant trend towards dose dependency in FMD improvement. The effects on other markers were minor and inhomogeneous. Based on these results it can be hypothesized that secukinumab has a beneficial effect on endothelial function in early atherosclerosis. With respect to other steps of developing of atherosclerosis, the study results can be considered inconclusive.

Date of Clinical Trial Report

30 January 2017